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The Journal will make an especial feature of the reviews of monographs and books bearing upon the field of Internal Medicine. Authors and publishers wishing to subject such material for the purposes of review should send it to the editor. While obviously impossible to make extended reviews of all material, an acknowledgment of all matter sent will be made in the department of reviews.

### Editor

ALFRED SCOTT WARTHIN, M.D.  
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Ann Arbor, Michigan

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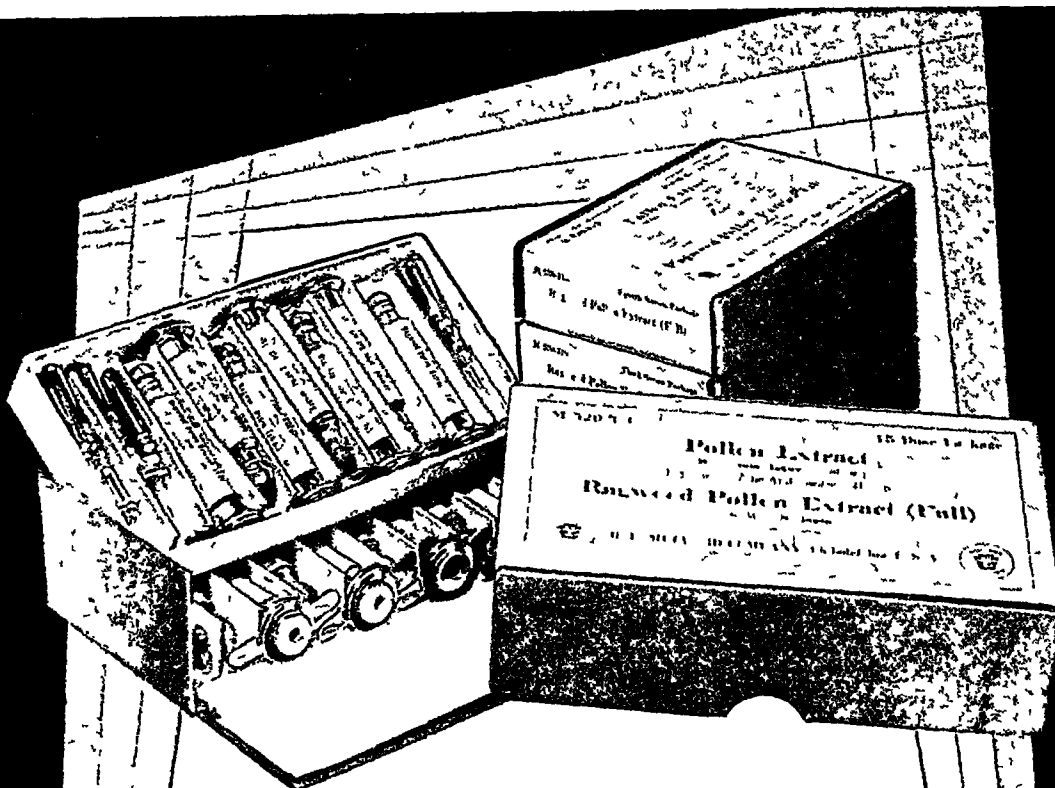
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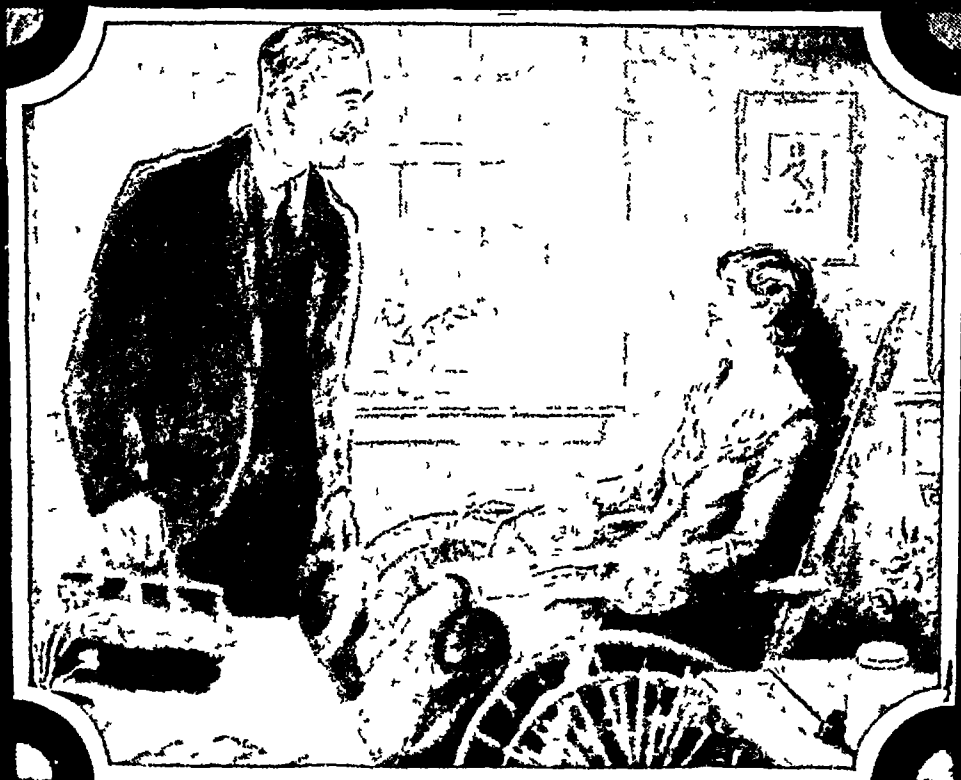
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By CHARLES F MARTIN, *Montreal, Canada*

**I** SPEAK no mere formal commonplace when I say that no man who has been made president of the American College of Physicians can feel other than deeply sensible of the honor conferred upon him, and humbly aware of the great responsibility which the acceptance of the office entails. When we remember that one of the finest assets of this Athens of America is its noble medical tradition and a great professional heritage and that the first president of this College was a graduate of Harvard University, we are warranted in feeling that a peculiar fitness attaches to our holding this convention here.

When the historian of American Achievement in the field of medicine shall tell the story of what has been done in medical teaching and in medical practice, he will assign a conspicuous place to Boston. For it was here that, early in the 17th century (indeed, not long after Wootton, the first practitioner of U S A put foot on American soil in 1607) that John Foster published the first American medical work. Here too was it not, that Dr Boylston of Brookline, as early as 1721 practiced inoculation against smallpox, opposed on the one hand by the great Benjamin Franklin and supported on the other, by the illustrious liberal preacher, Cotton Mather.

Then, as now in Boston, the Church joined hands with the medical profession in the treatment of disease.

Time fails me to carry the splendid Boston record through succeeding generations, let it suffice to make mention of some of the outstanding names emblazoned on the pages of contemporary medical records and destined to survive as long as medical history shall last,—Jackson and the Warrens the Bigelows and Homans, Bowditch and Cheever, the Shattucks, the Minots, the Morses, Cabots, Richardsons and a host of others.

Gentlemen, I fully realize that the honor you have accorded me is to be construed as a symbol of the cordial relationship that obtains and ever will obtain between the United States and the British Commonwealth even as between McGill University and the great educational institutions of the American Commonwealth.

We are assembled this evening to celebrate the 14th anniversary of this organization and in asking myself if I had anything to offer really worth the saying I was reminded of the couplet of Hageman

"Wisdom ripens into silence and  
the lesson she doth teach  
Is that life is more than language  
and that thought is more than  
speech



Yet I feel I should be false to the expectations of my associates and to the function of my office were I to practice the golden silence and withhold from you a *confessio fidei medicalis* and a frank expression of my cherished hopes for the future of this organization. Let me add that this involves no confession of sins or disclosure of secrets nor any memory of offenses. I make no mention of names but merely express personal views, the result perhaps of a too limited experience.

Our college has, as you know, developed through many vicissitudes and trials before reaching its present position, which, though materially advanced over earlier days, has not yet attained the consummation devoutly to be wished. Founded in 1915 under the corporate laws of the State of Delaware, it entertained for six or seven years an ardent hope of acquiring not only vigor within but also reputation without. This ambition, however, was slow in the coming. Clinical meetings, it is true, were held in various academic centers—meetings, however, which did not represent a spontaneous invitation on the part of universities to act as hosts to the College. Nor for a year or two did the foundation of an official journal materially advance the cause of the organization nor give to it either power or influence with the practitioners of Internal Medicine. It was indeed, not until 1922 that any distinctive advance was made, though even then the decorations of caps and gowns for Fellows, the frills and furbelows of solemn Convocations, the Rectors and Keys, the processions and ceremonies, succeeded but

little in advancing the reputation of the institution as a scientific, academic and professional organization of distinction.

While no records of these earlier years are available for reference, tradition tells of turbulent times, stormy meetings and disquieting incidents, together with questionable tactics to accomplish still more questionable ends—all of which did but serve to bring the College into disrepute and to make membership in it anything but desirable.

But soon new objectives were to be introduced and old ones more clearly defined. Under the guiding influence of President Stengel, great headway was made, more especially with respect to the fixing of definite qualifications for admission and improving the quality of membership, the formation of a Committee on Credentials endowed with judgment, tact and training—and fully conscious of its responsibilities.

The third stage of this evolution began with the Detroit Meeting in 1926, when a merger was effected with the so-called "Congress of Internal Medicine"—an organization whose sole object was to provide for an annual Clinical Meeting in various centers of the continent. Happily with this event and with the patient and untiring labor of my immediate predecessors in office, the more critical period was safely passed, and, I believe, today the threatened permanent mediocrity of the organization has given place to an assured position of growing importance and power, justifying as never before the exalted name which this College bears. And so,

despite the obstacles that may militate against it, an American College of Physicians is being worked out worthy of recognition by the profession at large and qualified to put on its members, as it were, a hallmark, guaranteeing both intellectual and moral equipment in the domain of internal medicine

No longer need the question be raised as to its justifiable place in our medical world. To the smaller and more exclusive organizations, many candidates, eligible though they may be, are not likely to attain, simply because of an established numerical limitation of membership.

The vast American Medical Association, on the other hand, with its section on medicine, its inclusiveness superseded as Dr. Vincent has said, only by the National Geographical Society, affords every practitioner the opportunity to benefit by what it offers, be it general or special, clinical or laboratory exercise. But it should be carefully noted that this section makes no effort to bring together those who specialize in internal medicine. Its peculiar value for the medical practitioner (and his sole qualification for admission) lies in contact with men of respectability in practice who pay the annual fee.

It becomes evident then that there exists no large organization on this continent which invites to its membership only practitioners of internal medicine men whose training has been specialized, whose desire for fuller knowledge is both deep and strong, and whose record is such as to confirm their fitness for participation in

a meeting to which only trained Internists are admitted.

Let me hasten to remind you that this is a volunteer organization which carries with it no compulsion. It makes no demands for the control of influence, nor does it represent that kind of a corporate body, admission to which is essential to academic or professional success. It has not presumed, and I trust never will presume, to dictate what shall or shall not be the essential mental equipment to insure university or hospital preferment. Its object is wholly disinterested, namely, the betterment of American Medicine by gathering together, in a brotherhood of medical sciences, men of worth and character, and ambition for a higher professional training.

Obviously such an organization as this will desire its members to possess character and a reputation that are beyond reproach and to be inspired by ideals compatible with the acknowledged aims of the College. This College invites to its membership first and foremost the leaders of the profession, who through precept and example, can add materially not alone to its prestige and its scientific contributions but encourage and stimulate the junior aspirants seriously striving for advancement in their profession. Its leaders should add their influence to keep the American College of Physicians worthy of its high-sounding name, for we cannot be true to the fact that this College with all its strength in numbers and in quality has come to stay.

On the other hand it makes its direct appeal to those who, during a brief training in the practice of medicine,

medicine, will ever keep before them the goal of admission and the opportunities it affords. It invites them to an appreciation of its aims and ideals. It further extends welcome more particularly to such trained internists who, while isolated from university life and larger contacts, aim at still greater advance and enlarged scope for achievement.

Nor has this organization, be it understood, ever intended, nor will it ever seek, to fill a place analogous to that of the Royal College of Physicians in London. There is no desire to inaugurate a meticulous series of examinations in the biological sciences, as a prerequisite for membership. Nevertheless we of this Institution do contend that, as the years go on, the younger practitioners of medicine desiring to gain admission must give evidence of an ever more thorough training in their specialty.

Let it be said moreover that we are differentiated from the American College of Surgeons in several particulars, to wit: a more modest ritual. It is not our intention to exercise any control or influence over hospital appointments or to assume any authority with regard to hospital administration except in a consultative capacity. The Board of Regents is selected with a jealous regard for the reputation of the College and in order that their prestige and character, and ability to administer its professional interests will redound to its permanent benefit.

*Matters Financial*—As there seems to be a misconception in some minds with respect to our financial aims and expectations let me digress for a few

moments and explain what these actually are. The officers, including the treasurer, have no desire to pile up for the College a golden treasure on earth, no ambition to accumulate, and no intention to secure large endowments as have some of our sister organizations,—nor is it our plan, insofar as I am aware, to build ourselves a permanent home or to establish philanthropies. On the other hand the American College, bearing as it does a national name, demands the appurtenances of dignity and should fulfil such physical requirements as will command the respect of every member of the profession. It is an organized institution which confers a certain benefit on its members *through* its organization, and so it must have its offices, its officials and staff, as also an adequate allowance to conduct its business. Beyond that it has no financial requirements or ambitions. Over and over again have we discussed the relatively large fees exacted for membership. Many of us would fain see them cut down or abolished; that some modification will be enacted in the near future is more than a pious hope. Let us never forget, however, that one of our most praiseworthy objects is to enable younger and less fortunate members, financially speaking, to win their spurs through the stimulus of the Organization. From them we demand a minimum fee *only* while those who are more fortunate and able to contribute to the Organization carry the load for these younger men. This is surely a real philanthropy and praiseworthy beyond contradiction. Let us further not forget that as our requirements are raised and our

standards made more rigid, our admissions will be lessened and our income diminished. Were it not for this we would venture at once on a drastic cut in fees.

*Reorganization*—In pursuance of a policy long considered, the College in its annual session yesterday initiated changes calculated to place the organization on a still higher plane. Not only will our Committee on Credentials scrutinize with added care the qualifications of prospective members, but after 1931 no candidate may be received into full Fellowship without having first traveled the somewhat steep and thorny road of probation as an Associate of the College. This important move implying as it does that greater and yet greater demands are being made upon the candidates for admission for Fellowship, will, it is confidently expected, add worth to the titles which this College has hitherto all too easily bestowed. Perhaps like Icarus with his waxy wings we are venturing too near the sun only to experience a similar dissolution of our strength and a fall to earth or sea. This I cannot believe—rather have we hitched our wagon to a star and maintained a loftier ambition and a higher ideal. Never was there a time richer in promise for the College, so replete with desire and opportunity to foster the scientific spirit. With Offi-

cers, Regents and Governors giving their heartwhole cooperation, little can go wrong with this organization. Some mistakes have been inevitable. Occasionally we have taken the wrong turn in the maze. Sometimes, like the actor on the stage, in a moment of light-hearted carelessness we have forgotten to tell the heroine the wine was drugged or the letters forged—or some other disaster arising directly from the frailties of human nature. It would be a miracle were it otherwise.

In retiring from the office to which you so magnanimously called me, and in bidding farewell to my colleagues on the Board of Regents, I most gratefully acknowledge my indebtedness, not alone for their cooperation and sympathetic interest at every turn, but also and still more for their unfailing tolerance and tireless patience under circumstances that were trying to a degree. And if I may express in a word my parting wish for this College, it is that by consecrated devotion to its cardinal aims, its value to the profession may become increasingly apparent and its prestige be such as to make those who are in it increasingly proud of their membership.

If only we are true to the ideals that we stand for, they will be true to us, and our College will forfeit none of its beneficent power but go on from strength to strength and from glory to glory.

syndrome has never been produced experimentally, although recent work<sup>42</sup> indicates that this may possibly be accomplished. Practically the only pathologic lesions of the suprarenal glands which one may expect to encounter are tuberculosis and simple atrophy, the former accounting for about 80 per cent of all cases. Authentic examples of the disease have been described as the results of (1) carcinomatous deposits in the suprarenal glands, (2) amyloidosis, (3) gumma, (4) destruction by hemorrhage or infarction with replacement by scar tissue, (5) chronic inflammation with secondary fibrosis, (6) mycosis fungoides,<sup>50</sup> and (7) lesions of the semilunar ganglions, celiac plexus, and the abdominal sympathetic chain without evident involvement of the suprarenal glands.

The latter group of cases, in which the suprarenal glands apparently have been normal, are found reported principally in the older literature. These reports are responsible for the long controversy which arose over the relation of the suprarenal glands to the Addisonian syndrome. It was firmly held by many authors that the seat of the disease lay in the sympathetic nervous system, rather than in the suprarenal glands. As the knowledge of hormones increased, this theory lost ground and it is now untenable, at least in an exclusive sense. However, cases recently have been described in which the Addisonian syndrome has been present with intact suprarenal glands.<sup>51,52</sup> Bittorf explains this phenomenon on the basis of injury to the secretory nerves of the gland. That irritation or interruption of the sympathetic nervous system is responsible

for some of the symptoms of the disease can hardly be questioned. Nevertheless, it is the opinion of modern observers that the essential basis for the syndrome which Addison described lies in the loss of function of the suprarenal gland alone.

The pathologic material from our series of cases has been studied by Barker. In twenty-six of the thirty necropsies bilateral, caseating tuberculosis of the suprarenal glands was revealed, in four, there was simple atrophy of the gland. Barker has also analyzed about seventy cases in which other suprarenal lesions were found at necropsy, these lesions include carcinoma, periganglioneuroma, amyloidosis, and hemorrhage. In none of this group did the clinical syndrome correspond to that described by Addison. Attempts have been made to establish a syndrome definitely related to the type of lesion present in the suprarenal gland. So far as we know, this is not possible, the cases with atrophy and tuberculosis run almost identical courses. It is of interest that pigmentation is more uniformly present in cases of suprarenal atrophy than in those in which the underlying factor is tuberculosis, also, on the average, length of life is apparently somewhat longer in the cases with atrophy. Otherwise the clinical course is practically identical in both groups.

#### THE FUNCTION OF THE SUPRARENAL GLANDS

Before beginning any discussion of the symptoms and signs of the disease we will refer briefly to the current theories of the function of the suprarenal glands. The gland consists of

two different portions which are of distinct embryonic origin and quite probably unrelated physiologically. The medulla of the gland consists largely of chromophil cells which are derived from the embryonic sympathetic system. Extirpation experiments show that it is not essential to life. The cortex is composed of epithelial cells arising from the wolffian body, the latter portion of the gland apparently is essential to life, as the experiments of Biedl, Wheeler and Vincent, Houssay and Lewis, Crowe and Wislocki, and others have shown. The medulla of the gland is the source of its only known active principle which is designated as epinephrine. There is a great deal of evidence, both anatomically and physiologically, that epinephrine normally enters the circulation by way of the central veins of the suprarenal glands and that it is concerned with the function of sympathetically innervated muscle and other tissues. The rate of discharge of epinephrine is not definitely established and neither is it certain that it is present in the circulating blood in sufficient amounts to exert its well known pharmacodynamic effects. Cannon suggested that epinephrine furnishes an emergency stimulant and that increased amounts are discharged into the circulation when the gland receives a stimulus as the result of fear, rage, hunger and so forth.

The cortex possibly yields some hormone which affects the growth of tissues and the organs of reproduction, it also may furnish even more vital substances since it is this portion of the gland which is essential to life. A possible antitoxic action of the cortex

has been suggested, and even as critical an observer as Stewart admitted that there is a possible physiologic basis for this hypothesis. Cortical extracts (which will be referred to later) are still in the experimental stage. A great many other theories have been advanced in regard to possible functions of the suprarenal glands and their relations with those of the other endocrine glands, but these theories rest on dubious ground and may be accepted only with reservations.

#### SYMPTOMATOLOGY

A better description of the disease has never been given than that advanced by its discoverer. "The leading and characteristic features of the morbid state to which I would direct attention are anemia, general languor and debility, remarkable feebleness of the heart's action, irritability of the stomach, and a peculiar change in the color of the skin. It may be said to present a dingy, smoky appearance of various tints or shades of deep amber or chestnut brown." With the lapse of time and the introduction of new diagnostic methods many additional points have been added to the symptomatology but reliance for diagnosis is still based on the symptoms mentioned by Addison.

We will confine our discussion in this paper to the general groups of symptoms and will attempt to give the current theories relating to their pathologic physiology. The cardinal symptom of this disease, asthma, was present in every case which we have observed. It is frequently extreme and the patient is unable to perform the slightest exertion without great in-

tigue The patient may be too weak to dress, to eat, or even to sit up in bed Studies with the ergograph show that the weakness is an objective as well as a subjective phenomenon An adequate explanation for the asthenia has not been offered In many cases (thirteen of thirty-eight in our series) the basal metabolic rate is definitely below the average normal Koehler<sup>36</sup> has studied patients with suprarenal insufficiency and has shown an oxygen deficit greater than that shown by normal persons performing the same exercises Hirsch and Capps have suggested a possible defect in utilization of oxygen as one of the symptoms of functional inadequacy of the suprarenal gland The relation of the sympathetic nervous system to this phenomenon is not known If one accepts Cannon's theory, asthenia may be explained on the basis of failure of production of epinephrine

The symptoms of secondary importance pertain to enfeebled circulation The signs which accompany this are well known, the apex of the heart rarely can be seen or felt, the heart sounds are faint and distant, the pulse is weak and compressible, and the blood pressure is usually low The latter observation is not as constant as one might expect, a point to which Janeway first called attention (fig 1) In at least 25 per cent of our cases the systolic blood pressure on the patient's admission was 105 mm of mercury or more In four cases in our series hypertension had been known to exist previously In one case the blood pressure was 145 systolic and 100 diastolic a week before death Ordinarily striking capillary or venous changes

do not develop even in advanced Addison's disease We have observed two cases, however, in which the veins of the forehead and upper arm remained persistently in a state of collapse, indicating marked reduction in venous pressure

The relation of blood pressure to posture in Addison's disease has not previously received the attention which it deserves Ghrist has studied patients on an adjustable table, and has shown that there is a definite postural element in the hypotension (fig 2) This, of course, accounts for the vertigo and faintness which many of these patients notice on arising from bed

The anatomic basis for the circulatory phenomena is fairly well established, the heart is usually considerably reduced in size and may exhibit brown atrophy It is not uncommon to find the aorta hypoplastic Curiously enough, in twenty-one of the twenty-five cases in our series in which electrocardiographic studies were made, abnormality was not shown In two cases significant T-wave negativity was found in one, auricular fibrillation, and in the other, arborization block In these cases there was a possibility of associated coronary sclerosis We have not been able to obtain figures on the cardiac output but there is every reason to believe that it would be considerably reduced It has been supposed that epinephrine is absent from the blood stream in Addison's disease<sup>30</sup> The experimental methods on which this theory is based are open to question, but from a clinical standpoint it is difficult to escape the conclusion that the hypotension and circulatory enfeeblement are due

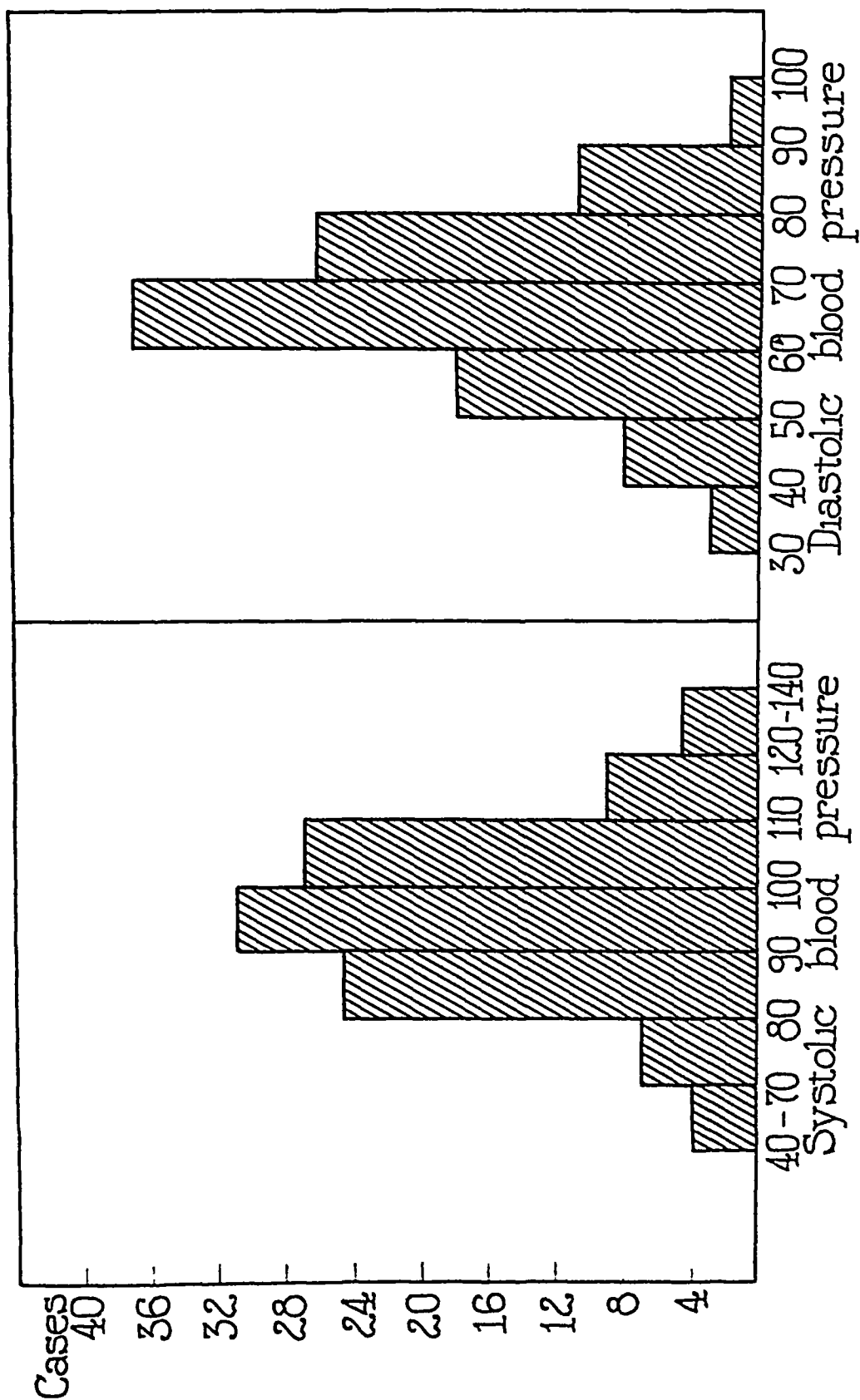


FIG. 1 Blood pressure readings in Addison's disease on patient's first examination



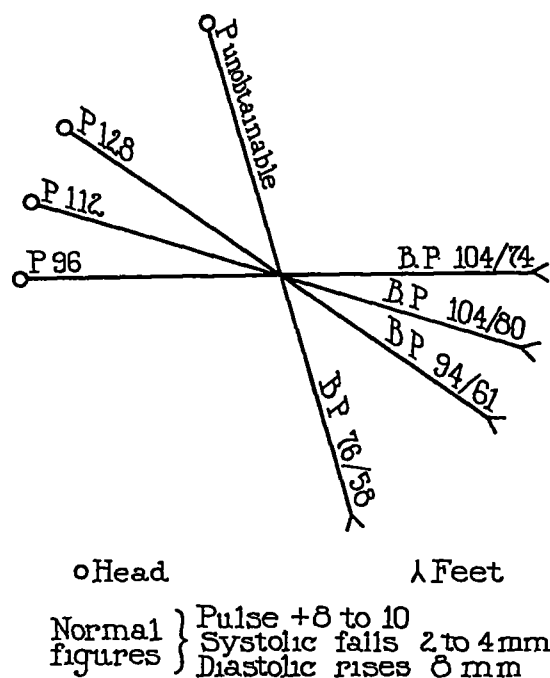


FIG 2 The effect of posture on blood pressure and pulse rate in Addison's disease

to lack of this pressor substance in the circulating blood

The nervous symptoms of Addison's disease are numerous and prominent. In our experience they have taken the form of sensory, motor or psychic phenomena. The most striking is mental irritability and restlessness, which gradually increases as the condition progresses. A sort of anxiety state is frequently observed. There may be actual delirium, and even acute mania. One of our patients suffered from somnambulism shortly before death; another died with acute cerebral symptoms suggestive of basilar meningitis. Coma is not uncommon and recovery from it is rare. In many cases the last days of life are spent in what appears to be a restless sleep. It is interesting to recall that terminal delirium is not infrequent in the experimental animal.<sup>41</sup> Numerous observers, including Pepper,<sup>42</sup> have described paresthesia of the extremities, and

we have noted two instances of early subacute combined degeneration of the spinal cord associated with the Addisonian syndrome. Although some of the nervous symptoms may be the direct results of anoxemia, an anatomic basis for them may exist. Degenerative changes in the central nervous system have been described, these consist chiefly of lesions in the posterior columns and nerve roots. Gordon<sup>44</sup> has described such a case and has reviewed the literature.

Pain in the back has been a most persistent and troublesome symptom. In many cases it has been the principal and earliest complaint. We have noted it in practically every case in our series, in many cases it has been disabling and severe. Tenderness on pressure over the costo-vertebral angles and hyperesthetic areas about the trunk are commonly present. Involvement of the sympathetic ganglion adjacent to the suprarenal gland may

be the cause of this pain, but frequently an anatomic basis cannot be found. Generalized neuralgic pains are also fairly common and may be due to actual neuritis.

In every case of Addison's disease which we have observed, gastro-intestinal disturbances of varying degrees of severity have been present. These vary from mild anorexia and nausea to violent attacks of vomiting simulating gastric crises. The abdominal wall may be rigid and tender even to the point of simulating peritonitis,<sup>17</sup> this has been known, unfortunately, to lead to surgical intervention. Vomiting is present in practically every case at some time and is often virtually uncontrollable; it is likely to recur with every exacerbation of symptoms. Retching, gagging and hiccup are common accompaniments. Epigastric pain is commonly associated with crises of vomiting, but may be present independently. Constipation is very common, in many cases it is an early symptom. Diarrhea in our experience has been almost exclusively a terminal symptom, and when it appears it has been most difficult to control. The inevitable result of the gastro-intestinal disturbances mentioned is loss of weight. We have not observed a single case in which loss of weight has not been considerable. Many of the patients do not appear to be emaciated, and the usual physical signs of loss of weight are not apparent, this may be at least partially due to the fact that a large number of our patients were overweight at the time the first symptoms of the disease were noted. The anatomic basis for these symptoms is not entirely clear, although

there are some observations on record which are of interest in this connection. As Mann, and Banting and Garms have shown, acute peptic ulcers are present in about two-thirds of all animals after bilateral supra-renalectomy. Lewin noted lesions of the gastro-intestinal mucosa in thirty-seven cases of his series, and various lesions of the liver and bile passages in 130. In our series of necropsies seven peptic ulcers were found and in four other cases roentgenographic evidence of duodenal ulcer was present. In two cases multiple acute gastric ulcers have been observed at necropsy. Whether the more chronic lesions represent cause or effect cannot be definitely stated, certainly the usual symptoms of peptic ulcer are infrequent. Hyperacidity is uncommon and when present it has been associated with the familiar syndrome of peptic ulcer. Anacidity was present in about half of the cases in which gastric analysis was performed, subacidity was noted in about 25 per cent of the cases. In our experience the administration of dilute hydrochloric acid first advocated by Grawitz has been of little if any benefit.

The relation of the abdominal sympathetic system to the symptoms just described is a matter for conjecture, perhaps interruption or irritation of these important nervous elements is responsible. Occasionally these gastro-intestinal symptoms are greatly relieved by the administration of epinephrine, perhaps more often the symptoms are not affected or are made worse by its use. If the pathologic physiology of these gastro-intestinal disturbances were fully understood,

most important portion of the problem of treatment might be solved

The most striking visible evidence of Addison's disease is the pigmentation of the skin. Although by no means always present, it is certainly the objective sign on which diagnosis is most frequently based. The depth of color is variable in the extreme, and in the literature one finds at least fifty adjectives used to describe it. The color most frequently seen is similar to that produced by sunburn but the color of many of the patients is actually negroid (figs 3 and 4). The exposed areas of the body are most deeply pigmented. There is also increased pigmentation over pressure points and in areas where the normal pigmentation is the most intense, such as the genitals, nipples and axillas. The skin is ordinarily soft and dry. Frequently there is a fine, grayish scurf over the knees and elbows. Pigmentation in the mouth is fairly constant (fig 5); the usual sites are the gums, the buccal mucous membrane, and the tongue. The lips are often deeply pigmented at the mucocutaneous juncture. We have attached a good deal of importance to pigmentary deposits produced by pressure from clothing. Tight waistbands, garters, corsets, shoes with straps, and hat bands may have produced a pigmentary deposit which makes the diagnosis clear. The pigmentation varies greatly in amount in different persons, and at different times in the same person. It often clears up remarkably during periods of improvement. During periods of decline tiny deposits of pigment are occasionally observed,

constituting the "black freckles" which have been so frequently described. In several of our cases, pigmentation was so slight as to attract little attention, in one case it was entirely absent. In two castrated persons, diffuse, yellowish pigmentation was present without the usual accentuation over the nipples and genitals. Leukoderma, first described by Addison, is fairly common. It is usually present in small isolated patches, but in two of our patients it was generalized and extreme. The color of the hair may deepen, and in many blond persons it assumes a strange, muddy color. Pigmentation of the conjunctiva, sclerotics and nails also has been encountered.

Like so many of the other phenomena associated with disease of the suprarenal glands, the cause of the pigmentation is not fully explained. The color of the skin is due to melanin, a normal cutaneous pigment. How and why melanin is deposited in such quantities is not known. Bloch and his collaborators<sup>8,9</sup> suggest that all pigmentation is due to the presence of a specific oxydase in the skin which forms melanin from dioxyphenylalanine. They believe that the latter substance, which they call "dopa," is one of the normal precursors of epinephrine, and that when formation of epinephrine fails in consequence of destruction of the suprarenal gland, these substances accumulate in the skin and are converted into pigment (fig 6). There is good evidence to show that the color of the skin in Addison's disease is due to a process of oxidation but the relation of dopa to the formation of epinephrine has not yet been proved.

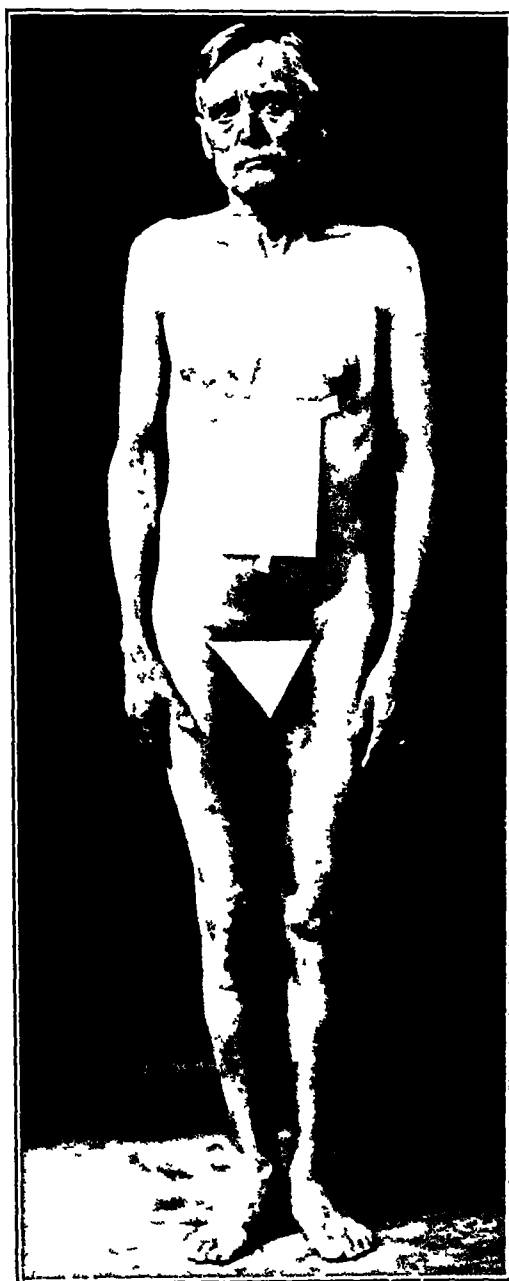


FIG. 3

FIG. 3. Pigmentation in Addison's disease.

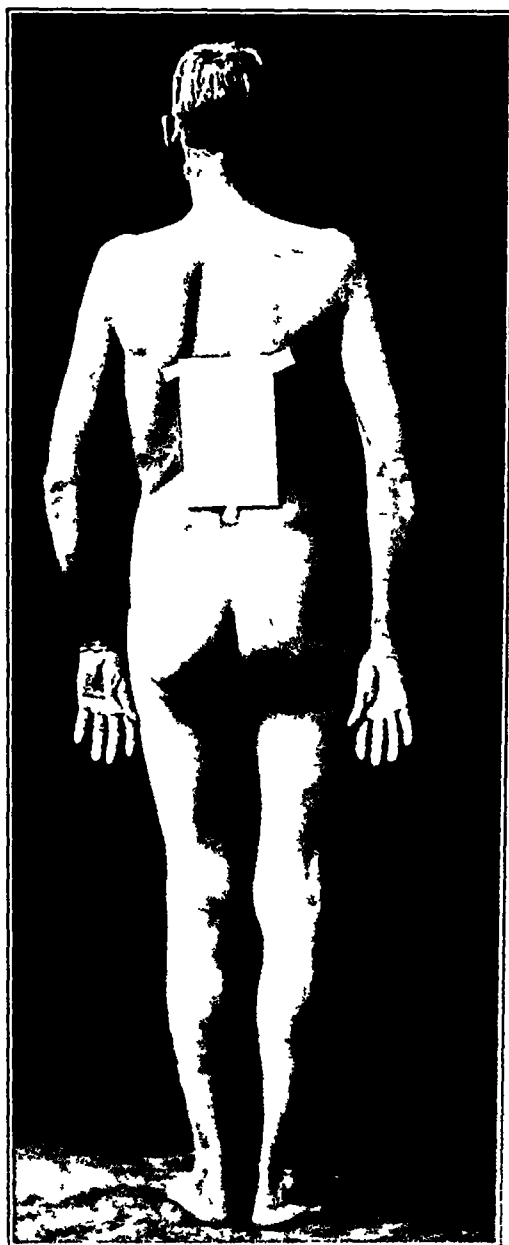


FIG. 4

FIG. 4. Same patient as that shown in figure 3. The appearance of the palms of the hands should be noted.

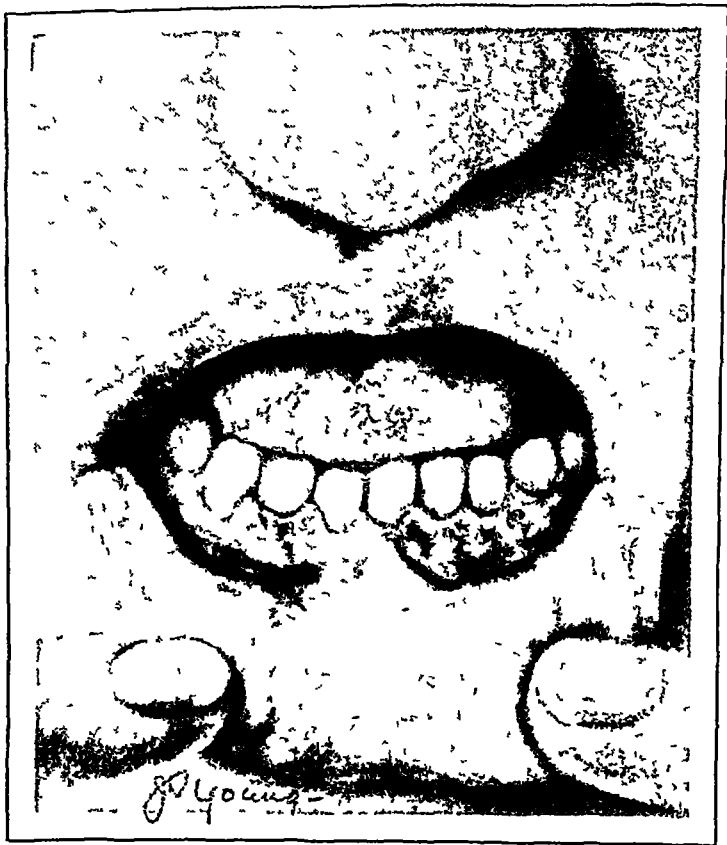


FIG 5 Oral pigmentation in Addison's disease

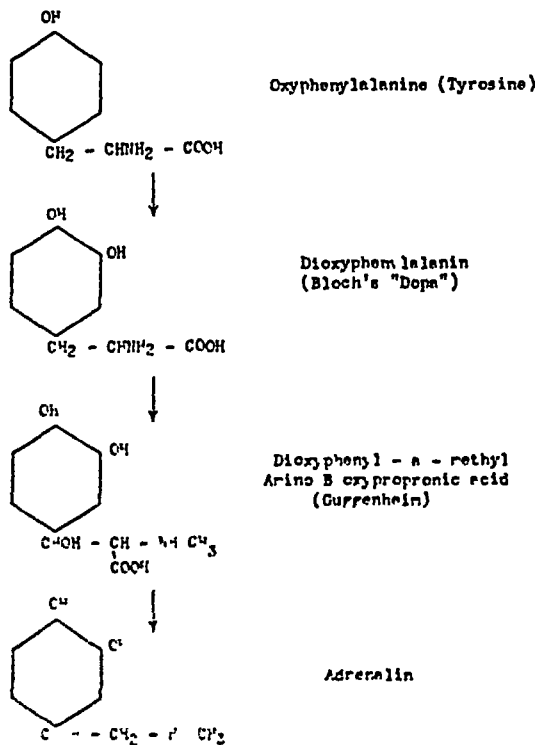


FIG. 6 Bloch's theory of pigmentation in Addison's disease (after Bloch and Joffler)  
'Dopa' when acted on by a specific oxydase is converted into melanin

## THE DIAGNOSIS

Few diseases can be diagnosed with greater certainty when the typical signs and symptoms are present. This fact is attested by the observation of many writers. When the disease is present in an advanced and typical form, the opportunities for diagnostic errors are small, in our experience the negative errors greatly outweigh those of a positive nature. As Tuckwell (1871) said, "There is no neurosis nor is there any accidental melasma which simulates the true addisonian symptoms so closely as not to be distinguishable from them by trained observation." Doubtful and atypical cases are an entirely different matter, and in this group a positive diagnosis is frequently impossible, a period of observation in hospital is valuable. We are not familiar with any definite pathognomonic signs, the white line of Seigent has not been a constant sign in our cases.

Laboratory examinations are not of great diagnostic value, although they may furnish corroborative evidence. Urinalysis and renal functional tests almost invariably show evidences of renal involvement. Low specific gravity of the urine is the rule, variable amounts of albumin and occasional casts also are found. Elevation of the blood urea is common, particularly in the terminal stages, this is in accord with the observations after experimental suprarenalectomy.<sup>12</sup> The urinary output is frequently low before death, and in fact there may be suppression of urine.<sup>13</sup> These phenomena perhaps can be explained on the basis of a deficient blood supply, and are very suggestive of those seen in arteriosclerotic

nephritis. Barker has observed tubular atrophy and other signs of toxic nephrosis at necropsy, in Smith's case the picture was somewhat similar. Blood counts rarely give significant information.<sup>14</sup> Anemia, contrary to Addison's opinion, is rare and when present is usually to be explained on the basis of some complication. Signs of increased concentration of the blood may be present in the terminal stages and are a grave prognostic omen. The total blood volume, as Brown and Roth have shown, is not usually affected except in terminal conditions with the picture of shock. In suprarenalectomized animals increased concentration of the blood may be observed shortly before death.<sup>15,16</sup> Relative lymphocytosis has been mentioned by many authors and has been present in several of our cases but we do not regard it as an infallible diagnostic sign. It has been attributed to the lymphoid hyperplasia so frequently observed at necropsy. Changes in the metabolic rate in the electrocardiogram, and in the results of gastric analysis already have been mentioned. We have examined the blood cholesterol and blood calcium in a number of cases but any changes observed have been slight and inconstant. Hypoglycemia regarded by some German authors as a characteristic feature has been present in a few of our cases as a terminal phenomenon. We agree with Roscnow and Jaguttis that it is not a pathognomonic sign nor even constant in its occurrence.

The demonstration of tuberculosis elsewhere in the body is of great importance and the search for it should be thorough in every suspected case.

As has been stated, it is demonstrable in about a third of all cases. Biopsy of the skin is valuable so far as it excludes other types of pigmentation.

In doubtful cases diagnosis is best made by exclusion and by a period of observation in hospital.

When hypotension, hyperpigmentation, gastro-intestinal symptoms, and asthenia are present without any apparent cause, the probability of suparenal disease is very great. In our experience this diagnostic triad has been of the gravest prognostic significance, in the majority of the cases in which we have suspected the disease to be present, but which were not included in this series because of atypical features or insufficient observation, death is known to have occurred.

#### THE COURSE OF THE DISEASE

The course of the disease is variable, its duration varying from eighteen days<sup>10</sup> to sixteen years.<sup>6</sup> The extremes in our series were six weeks and seven and a half years, the average duration was somewhat less than two years. The order in which the symptoms may appear and the rapidity of their development also are variable. In general we recognize four types of cases following Greenhow's classification: (1) cases in which the pigmentation, asthenia and other symptoms develop simultaneously, and run a more or less parallel course, (2) cases in which pigmentation is present for some time (often for several years) before the development of other symptoms, (3) cases with asthenia and gastro-intestinal symptoms and with pigmentation which develops

late in the course of the disease, and (4) latent or atypical cases.

It is well known that the disease is marked by periods of remission and exacerbation, although these periods are by no means always present. In general the disease appears to progress by spurts, interspersed with periods when its course seems temporarily arrested. The periods of decline are almost invariably attended with severe gastro-intestinal symptoms, and in fact one can judge the progress of any given patient by his ability to take and retain food.

The manner of death in Addison's disease is sufficiently striking to present an almost unmistakable clinical picture. In many persons whom we have observed the terminal symptoms have appeared suddenly, in others they are preceded by a prolonged, gradual decline. The terminal phenomena are not greatly different from those seen in the experimental animal after supra-renalectomy. Gastro-intestinal symptoms, principally vomiting and diarrhea, almost invariably are present. Restlessness, at first extreme, later progresses to a muttering delirium and coma. Terminal pyrexia is not uncommon, hyperpyrexia was recorded by Lucas. The terminal condition has been likened to the flickering of a dying flame, but the time of death may be very stormy with convulsions and pronounced cerebral symptoms. Sudden death, which has been compared with that caused by coronary thrombosis, is not infrequent.

The blood pressure may be maintained at a fairly constant level until late in the course of the disease, the pulse rate rises as the blood pressure

declines Figure 7 shows the temperature, pulse and blood pressure in a typical case

There is much about the terminal picture of Addison's disease to suggest intoxication, this view has been advanced by workers in the experimental field, and the parallelism in the terminal phenomena in dogs and in man

seems to point to a possible antitoxic function of the suprarenal cortex Stewart, speaking from a physiologic standpoint, believes that the central nervous system is most heavily involved in this terminal intoxication, and certainly our clinical experience supports this view The possibility of other organs being injured by this

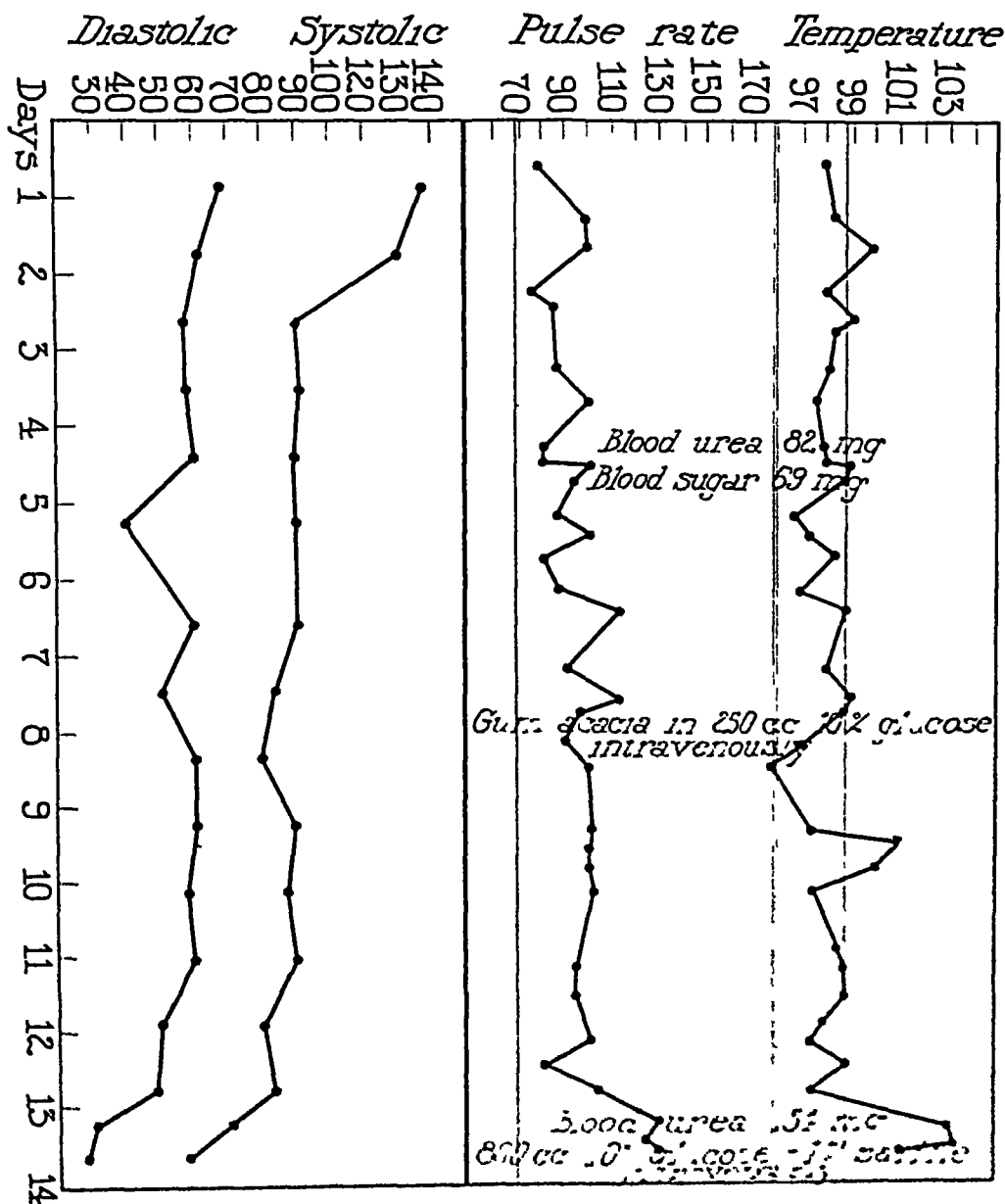


FIG 7 Clinical chart in a fatal case of Addison's disease



toxic process also was suggested by Stewart, who mentioned the known incidence of renal functional failure as possible evidence on this point

The complications of the disease encountered in our series are of considerable interest since they frequently confuse the clinical picture and lead to great difficulties in treatment. Tuberculosis was present in thirty-six of the cases in our series, active pulmonary tuberculosis was present in seven of these cases, inactive pulmonary, in ten, genito-urinary, in thirteen, osseous, in eleven, glandular, in two, cutaneous, in one case, and a tuberculous lumbar sinus in one case. In four cases each of the series, syphilis, preexisting hypertension, and peptic ulcer was present. In one case each of the series cholelithiasis, Paget's disease, myxedema, diabetes mellitus and exophthalmic goiter combined, gout and coronary sclerosis combined, and pernicious anemia was present.

Tuberculosis, of course, leads the list, symptomatically active pulmonary tuberculosis, however, is not as common as one might expect, genito-urinary and osseous tuberculosis are observed more frequently. Five of our patients had advanced Pott's disease, in two cases there was active tuberculosis of the cervical lymph nodes. Abnormalities of the other glands of internal secretion were not commonly observed. In one proved case exophthalmic goiter and diabetes mellitus were present. Both complications are rare, diabetes associated with Addison's disease has been observed by Arnett and by West, and exophthalmic goiter by Etienne and Richard. In our case the pigmentation was slight,

the blood pressure was normal, and the asthenia was not greater than might be accounted for by the hyperthyroidism. After thyroidectomy the patient declined rapidly, and died in spite of active supportive treatment; at necropsy marked atrophy of the pancreas and suprarenal glands was found. Another patient had as a complication definite myxedema with a metabolic rate 31 per cent below normal. He did not improve in the slightest under treatment with thyroid extract and he died with a definite picture of Addison's disease. Maish has recently described a somewhat similar case. A third patient presented the hitherto unrecorded combination of pernicious anemia and tuberculosis of the suprarenal glands, the Addisonian syndrome appearing as a terminal event. Sections of the suprarenal glands contained large numbers of bacilli of tuberculosis. This case is of great interest because of the views of Addison in regard to the relation between disease of the suprarenal glands and primary anemia. Paget's disease also was diagnosed in one case in which a typical Addisonian syndrome was present, this is a heretofore unrecorded complication, although Leib and Pepper have both described bony changes in the disease. The incidence of peptic ulcer has already been mentioned.

#### TREATMENT

The treatment of Addison's disease has always been a thankless and difficult task, as in many other intractable conditions just enough good results are obtained to justify continued effort. Radical curative measures are

practically unknown, Oestreich, however, was successful in removing a tuberculous suprarenal gland in a case in which a definite addisonian syndrome was present, the other suprarenal gland apparently was normal. Transplants have been disappointing, the surgical risk appears to be large and the possibility of a "take" small. Irradiation of known tuberculous suprarenal glands was first practiced by Golubinin (1905) and according to Desjardin's recent review can do little harm to the suprarenal tissue, it may stimulate healing of the tuberculous process and thus offers some prospect of cure. We have employed this treatment in four cases recently, untoward reactions did not occur, and all the patients are doing well at present. As Barker has shown, tuberculosis of the suprarenal glands shows little, if any, tendency to spontaneous healing, it may be that in some instances at least, irradiation will stimulate formation of fibrous tissue and check the pathologic process. Tuberculin has hitherto failed to accomplish this, and too much

should not be expected of radiotherapy.

There is evidence that Addison's disease may be of syphilitic origin, but such cases must represent a small minority. Apparent cures have followed antisyphilitic treatment.<sup>61</sup> Two of our patients who gave histories of recent syphilitic infection have received antisyphilitic treatment elsewhere with fairly good results, although one had numerous reactions from treatment, in a third patient who was known to have syphilis, atrophy of the gland was found at necropsy, death was apparently precipitated by a severe reaction following the administration of bismuth. Judging from our experience the treatment of syphilitic patients with the addisonian syndrome must be carried out with a good deal of caution.

Substitution organotherapy is as old as the disease; the earlier results have been reviewed by Kinnicutt, Johnston and Adams, who have each reviewed the literature and summarized the effects of treatment (table 1). Many of the cases are duplicates and the cri-

TABLE 1.—RESULTS OF SUBSTITUTION ORGANOOTHERAPY AS REPORTED BY OTHERS

Author	Cases	Condition Worse	Condition Unimproved or Patient Died	Temporary Improvement	Prolonged Improvement	Comment
Kinnicutt	48	2	18	22	6	One patient well for four months, one for twelve months, and one for eighteen months.
Johnston	50		10	16	10	Results not stated in eight cases.
Adams	105	7	40	33	16	One patient each lived two, three, four and eight years.

teria for improvement or arrest of the disease are of course not uniform. Many of the patients reported as improved had been under observation only a few weeks.

Our interest in organotherapy in Addison's disease began in 1920, when the regimen now in use was instituted in the case of the late Dr Muirhead. This form of treatment, which has since been fully reported by Muirhead and by Rowntree,<sup>58</sup> consists of the administration of epinephrine hypodermically, and by rectum to the point of tolerance, together with suprarenal cortex\* by mouth in full dosage. The effects of organotherapy in sixty-two cases of Addison's disease in our series were as follows: the condition was made worse by treatment in one case, benefit was not derived in twenty-nine cases, slight or doubtful improvement for six months or less occurred in thirteen cases, temporary improvement for six months to a year in six, temporary improvement for one to two years in two, and definite improvement for two to five years in nine, in two cases the disease is believed to be arrested since there has been absence of symptoms for five to eight years.

We freely admit the theoretic and practical imperfections of this form of treatment, and are not enthusiastic about its results. However, it offers palliation of symptoms in some cases, and prolonged benefit in a small percentage of cases. Many of the patients listed as "temporarily improved" have made remarkable and unexpected improvement only to die later from intercurrent infections.

The effects obtained are usually noticed at once, and we believe that unless some improvement is noticed within a week, further active treatment is not to be urged. Organotherapy appears not to be of value in the terminal stage of the disease, but it has certainly prolonged the life of many patients who were in a very critical condition at the time of admission. The patients who have obtained prolonged benefit are, of course, few in number. In two of our proved cases of atrophy of the supra-renal glands, treatment was carried out for three and four years respectively. The patients felt well and were able to carry on their usual occupations to within a few days of their death. One of them had given up treatment on two occasions and at once alarming symptoms had developed which were relieved by the resumption of the administrations of epinephrine. Among the patients in our series known to be living, one has survived three years, and when last heard of was in good condition. Another patient has had the disease for more than four years, he is able to work regularly, and although definite pigmentation is still present he feels well. A third patient has been treated for more than two years and is able to carry on her duties as principal of a high school. A fourth patient, a man of fifty-two years who lives near Rochester, has been under observation constantly for seven years. He has no complaints except that he is easily fatigued and has some backache. He has been able to carry on his farm work. A young man who was first seen in 1922, is apparently well and has discontinued

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\*Supplied by Parke Davis and Co.

treatment In patients who have survived over such long periods, the accuracy of the diagnosis may be questioned, the syndrome in each of these cases was absolutely typical, however, and we regard the cases as authentic examples of the disease

The effect of treatment on symptoms is worthy of brief mention The pigmentation fades perceptibly in many favorable cases, as we have been able to show by a study of color patches, the gastro-intestinal symptoms subside, and there may be gain in weight A definite gain in strength is also noted in many cases, certain patients are able to resume their usual occupations It is almost impossible to maintain elevation in blood pressure in Addison's disease over any considerable period of time, substances that cause increase in blood pressure produce elevation which is of short duration at best Ephedrine will cause elevation and maintenance of the blood pressure more satisfactorily than other substances we have used, but there is no evidence to show that it produces any lasting general improvement<sup>60</sup> We have regarded 75 mm of mercury as the critical level for systolic blood pressure in this condition, when lower levels than this are reached death is imminent and nothing can be expected from stimulants of any sort

The terminal symptoms of Addison's disease do not respond to any treatment with which we are familiar The preterminal phenomena the crises, and periods of acute exacerbation are scarcely less resistant These episodes in the course of the disease recall to mind the theory that some toxin may be responsible for their pro-

duction Perhaps the best treatment in emergencies is the intravenous administration of fluids Rogoff and Stewart,<sup>73</sup> Corey and others have repeatedly demonstrated the value of the administration of Ringer's solution intravenously to prolong the life of suprarenalectomized animals There is no doubt that the intravenous administration of solutions of salt or glucose has been of temporary benefit to patients with Addison's disease, and we have found it a most useful procedure Gum acacia has been helpful in states of shock

There is one form of treatment of Addison's disease which has not received the attention it deserves the protection of the patient from every outside influence which will exhaust his strength or tire him unduly Purgation has been known to cause an immediate fatal termination We have observed three such instances The transportation of a patient over any considerable distance is frequently followed by serious results We have observed several fatal events which have been precipitated by such a cause one patient died forty-five minutes after her arrival in Rochester and another survived about twenty-four hours Exhaustive examinations also have led to the development of serious symptoms Careful supportive and protective treatment should be the first consideration in every case this has a prior claim over organotherapy, irradiation, and every other diagnostic or therapeutic procedure

It is natural to suppose that treatment directed toward the related associated diseases might have a beneficial influence on the course of the

primary disease This supposition would seem particularly justified if these complications were of a tuberculous nature Unfortunately, this is not the case, surgical intervention in glandular, osseous or genito-urinary tuberculosis is associated with a prohibitive risk The complicating diseases that have been noted have masked the diagnosis in eight cases of our series and in each of these latent or atypical cases surgical procedures have precipitated a fatal outcome Only three patients in our series survived surgical operations of any kind (table 2)

Our experience with complications of Addison's disease can be briefly summarized by saying that attention

to these may, as it did in one of Addison's cases, lead to neglect of the primary condition, that the correct diagnosis is frequently missed because of their presence, and finally that treatment of the complicating lesion is not likely to be of benefit If treatment necessitates any surgical procedure the risk is prohibitive and should not be assumed

With treatment of all kinds, our experience has been distinctly unfavorable This is perhaps to be expected when one considers the fate of the suprarenalectomized animal and recalls that at necropsy in Addison's disease the suprarenal glands are almost always completely destroyed A few cortical adenomas may remain, but

TABLE 2—RESULTS OF OPERATION

Case	Sex and Age	Asthma, Grade	Pigmentation, Grade	Blood Pressure		Operation	Comment
				Systolic	Diastolic		
1	M34	2	0 to 1			Amputation of right leg	Death
4	M37	1 to 2	1 to 2	130	90	Thyroidectomy	"
10	M32	0 to 1	1 (racial)	105	75	Hemorrhoidectomy	"
11	M25	2	1 to 2	100	80	Orchidectomy	
19	M65	1	1	110	78	Nephrectomy	"
20	M26	1 to 2	2	105	75	Nephrectomy	"
27	M46	2+	2	108	78	Cholecystectomy	"
32	F 32	3	2	75	?	Nephrectomy	"
13	F 54	2	3	80	60	Drainage of lumbar abscess	Survived
73	F 54	2	2+	90	70	Tonsillectomy	"
88	M52	2	2+	100	75	Excision of cervical lymph nodes	"

there is usually little, if any, evidence of functioning suprarenal tissue. It would appear to be possible to maintain life as long as a small fragment of cortex remains, but up to the present time cortical or medullary extract has not had the effect of maintaining life indefinitely when the suprarenal glands are totally destroyed. The greatest promise of success in the treatment of Addison's disease lies in the work that is being done independently by Rogoff and Stewart,<sup>54</sup> Koehler,<sup>55</sup> and Hartman, McArthur and Hartman in the preparation of cortical extracts. Ro-

goff's "cortin" has prolonged the lives of suprarenalectomized dogs and Hartman's extract has given similar results in cats. We have not had personal experience with the use of these extracts, which are still in the experimental stage, they may prove to be of great value in clinical cases, and will be a welcome addition to our limited therapeutic resources. In view of the known progressive character of the pathologic lesions, however, one may anticipate a high mortality even with theoretically perfect substitution therapy.

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# Observations on Tuberculosis in Europe—Special Methods of Treatment, Government Schemes\*

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THESE notes were made while in Britain and Europe last autumn as a member of the Canadian Tuberculosis Association tour. We were a party of thirty-two Canadian physicians, all interested in tuberculosis. The party was made up chiefly of sanatorium superintendents, directors of chest clinics, and chiefs of provincial diagnostic services representing every province in the Dominion.

Opportunity was offered our party to see the methods of treatment followed in sanatoriums which were visited in England, Wales, Scotland, France, Switzerland and Italy.

As with us the underlying principle of treatment for both pulmonary and non-pulmonary forms of tuberculous infection was prolonged rest of the affected organ while the lesion was active, this period followed by exercise when the disease was definitely quiescent.

Heliotherapy and aerotherapy were valuable adjuvants. Everywhere we found a great interest in collapse therapy (pneumothorax) and thoracoplasty, as aids in treatment of pulmonary tuberculosis, accessory methods of treatment which are consid-

ered as the greatest contribution to the therapy of pulmonary disease made in recent years.

The treatment of the so-called surgical forms of tuberculosis—bones and joints, lymphadenitis, cold abscesses, etc—is not carried out to any extent at the present in general or surgical hospitals but rather in sanatoriums and special open air orthopedic hospitals. We saw many such institutions in and about Glasgow, Lanark County, Edinburgh, Liverpool, Cardiff, South Wales, Alton, Hayling Island, Oxford and Cambridge, as well as on the continent. Light therapy both natural and artificial with aerotherapy is everywhere used in bone and joint cases, and striking results were presented to us. I need not give the details of treatment. They were admirably presented to the profession here by Sir Henry Gauvain two years ago. Artificial light therapy is extensively used in Britain where sunshine is not available every day and the therapeutic rays are almost absent from sunshine for a relatively great portion of the year. Exposure of the body to the air seems to have marked beneficial effect apart from the direct light therapy. Practically all of the British institutions have well equipped

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artificial light equipment which is used in the bone and joint cases and abdominal tuberculosis

I would like to quote here the concise statement prepared for our party by Dr. R. J. Collins of River Glade, N. B.

"The use of artificial means of light treatment was universal, particularly in the extra pulmonary group. The majority preferred the simple carbon arcs of 30 and 75 amp with uncomplicated feed. The advantage over the mercury vapor lamp seemed to be in the fact that more patients could be treated at one time and that experts doubted that the emanations from the mercury arc were as effective as from the naked carbon. The cost of current supply is however greater per machine unit but probably the same per individual treatment.

"The Finsen lamp was particularly adaptable for lupus but inasmuch as it is seemingly a rare disease with us, the ordinary institution is not advised to purchase this outfit. It is expensive and requires a highly efficient personnel.

"Other forms of arc lamps were passed over as without particular value. After our experience in Scotland wherein simple aeration was considered very effective, it throws some doubt on the highly advocated use of the artificial and natural sun treatment. It has been suggested that further experimentation be undertaken throughout Canada to settle some controversial points.

"It seems fitting to end up this discussion by issuing a word of caution to the public in the over use and indeed dangerous use of such powerful

agents as the sun and various artificial light treatments. The present sun craze has this to recommend, however, that people from all walks of life will lead a healthier outdoor life, but on the other hand we would point out that this treatment in tuberculosis must be under the supervision of trained personnel."

We learned that much harm has been done by injudicious application of light therapy. Living and sleeping in the open air was everywhere accepted as routine in pulmonary tuberculosis but light therapy was not considered to be of particular benefit by most of the sanatorium physicians we met.

*Prevention of Tuberculosis* We were given opportunity in France to see the application in practice of two methods devised for the prevention of tuberculosis, one of approved merit, *Placement Familial*, the other with as yet value unproven *Vaccination with living tubercle bacilli*. For many years there has been an attempt in many parts of France to carry out Grancher's work of prevention in removing from their homes at birth the children of tuberculous mothers. Recognizing the great morbidity and mortality in children born of tuberculous mothers if kept in contact, and in infants living in a home with an open case of tuberculosis, Grancher many years ago devised and practiced his method of caring for such children in foster homes. L'Oeuvre du Placement Familial des Tout-Petits has developed the Grancher method by caring for such children in foster homes in the country grouped about a dispensary centre in a village. To this dispensary are at-

tached a physician and nurses who see the children at regular intervals, carry on the work of a well baby clinic, supervise the foster homes, and use the hospital beds in the dispensary in case of illness whether of infectious dietetic or other origin. These dispensaries are able to care for some 600 children from the city of Paris or the Department of the Seine. Children are received from birth to two years of age and are kept there till their fourth year.

Some nine dispensaries are in operation supervising from thirty to ninety children each. The report for 1928 shows 505 children cared for with 8 deaths from all causes, five deaths in the dispensary centres and three deaths in children in the first month after leaving the centre. This is a remarkable showing, and indicates what can be done by removing children from their infected environment and placing them under hygienic conditions in properly supervised homes.

Vaccination with living tubercle bacilli as a means of developing immunity against tuberculosis has been extensively adopted in France and the French Colonies following the introduction of the B C G vaccine of Calmette and Guérin. This vaccine is from a culture of living bacilli from a strain said to be non-virulent and non-tuberculinogenic. It is prepared by the Pasteur Institute and is good for ten days after issue. It is administered orally to infants in the first ten days of life, though some clinicians have been using it subcutaneously in children up to 20 years who give no reaction to tuberculin and who are free from all clinical and radiological

signs of tubercle infection. To infants it is given in three doses as soon as possible after birth, for example on the 3rd, 5th and 7th days or on the 6th, 8th and 10th. One or two doses is not considered sufficient. Revaccination of exposed children is advised at the end of their first and third years.

Up to the beginning of 1928, 52,772 infants had been vaccinated at birth, in France. Of these 5,749 were born of tuberculous mothers or living in an infected home. General Jourdan, formerly Director of Public Health in Tonkin and in other French Colonies, told us in London that 50,000 vaccinations had been registered in French Indo-China. It has not been adopted in England. Prof Greenwood has shown that the French statistics thus far presented are unsatisfactory, and the impression we received of the general opinion in England was that the prophylactic value of B C G is not proven. In Italy Prof Ascoli of Milan has recently reviewed the experimental work done on vaccination against tuberculosis, including B C G. He regards the results as favorable. Yet an English reviewer of his work does not consider his tests on infants to be very convincing. The opinion in America as well as in England appears to be that further work will have to be carried on in several directions before finality can be reached. There is a generally expressed hope that further and better tests may decide its efficiency or otherwise. Petroff has recently expressed the opinion that the use of B C G in prophylactic immunization may be a dangerous procedure but states he is open to a change of opinion if further experience

that his interpretation of past studies should prove erroneous. Some have expressed the fear that these non-virulent and non-pathogenic forms, if long present in the human body, may regain their virulence. Tubercle bacilli may survive in the body for many years. And we know that some forms of pathogenic bacteria which have been rendered non-virulent by repeated subculturing, may regain their pathogenic qualities by a passage through animals.

*Sanocrysin* In 1924 Moellgaard announced that sanocrysin when given sufficiently early in adequate amount, exercises a strikingly beneficial effect on tuberculous lesions in calves. Clinical workers soon applied it in human tuberculosis with some striking results beneficial and otherwise. In large doses severe and even fatal results were recorded. With some workers enthusiastic, others felt it was a dangerous drug the use of which could not be safely advised. Two years ago Prof. Lyle Cummins reported in this hall some experimental work which seemed encouraging. Seeking information as to its clinical use in Great Britain we found a number of men were studying its effect on clinical tuberculosis in man. It would seem that we are approaching the point when tabulating results may give us useful information as to its application.

*Sanocrysin* is an aurothiosulphate of sodium with formula  $\text{Au} (\text{S}_2\text{O}_3)_2 \text{Na}_2$ . It is claimed for it that it has a selective affinity for tuberculous lesions, is extremely soluble in water, rapidly diffusible and is stable, being very slowly decomposed in the body without formation of toxic substances.

It is a snow white salt crystallized in fine needles. Kept in sealed ampoules it appears to be stable for a year. A 1 in 100,000 dilution prevents growth of tubercle bacilli *in vitro* and in 1 in 1,000,000 growth is retarded. The dosage used varies with the individual, sex, age, weight and presence or absence of fever. Ten or twelve intravenous injections at intervals of 3 or 4 days may constitute the first series. In 6 to 8 weeks a second series of intravenous injections follows at intervals of about four days. If necessary a new course may be given in four or five months.

It is not advised in patients with extensive fibrosis but rather in patients with a recent lesion, whether minimal or early or whether a recent extension in a case of old standing.

A very good summary is that given by Heaf in *Tubercle* of December, 1927, in which he concludes

1 That results are not sufficiently certain to warrant use before routine or collapse therapy has been tried

2 That the contraindications are such that only a small percentage of cases are suitable for treatment

3 If given, dosage should produce only slightest reaction or none

4 More knowledge as to its elimination is needed before it can be considered safe treatment

5 Some cases make remarkable progress and the majority improved, but the action of the drug was so irregular as to make it impossible to predict a good result

6 The most constant successes were in cases where the treatment was used to supplement collapse therapy

7. It may be used in children

For its use a patient must have  
 1 good physique, 2 healthy liver and kidneys, 3 no bronchitis, emphysema or extensive fibroid disease, 4 little toxemia, 5 a moderately early lesion or recent extension of an old one, 6 no tuberculous enteritis

He reports 50 cases, of whom

16 clinically arrested

12 improved and have not relapsed

5 improved but have relapsed

10 no improvement but not worse

2 made worse

5 died as result of treatment

Further knowledge of its administration and contraindications have lessened the mortality rate

*Government Schemes* We found that the Governments of Great Britain, France and Italy have each developed a definite scheme to combat tuberculosis, through government assistance to diagnostic and treatment dispensaries, sanatoriums for pulmonary cases and hospitals for non-pulmonary forms of tuberculosis

Great Britain in framing its plan for the administrative control of tuberculosis adopted the Tuberculosis Scheme for the prevention and treatment of tuberculosis recommended by the Departmental Committee on Tuberculosis in 1912-13. This includes essentially two factors, namely:

(1) THE DISPENSARY UNIT consisting of Tuberculosis Dispensaries with staff of officers and extensive and varied operations for the detection and prevention of tuberculosis

(2) THE INSTITUTIONAL UNIT, consisting of Sanatoriums, Hospitals, Training Colonies, Open-air Schools, etc

The control of tuberculosis constitutes an important department of Public Health Administration. It is now the duty of Councils of Counties and County Boroughs (in Scotland, Local Authorities, or combinations thereof), to formulate Tuberculosis Schemes for their several areas. The Schemes are submitted to the respective Ministry of Health or Board of Health (Scotland). With the Ministry or Board, as final Health Authority, rests the responsibility of endorsement and formal approval. Such approval carries with it a contribution from the State of 50 per cent towards capital outlay and annual maintenance.

It may be recalled that Notification of cases of tuberculosis is, by statute, compulsory throughout Great Britain. Notification of pulmonary tuberculosis was made compulsory in 1912, and, after two years trial of the system, compulsory notification was, in 1914, extended to all forms of tuberculosis.

A complete Tuberculosis Scheme includes the operations of a Care Committee.

The work in each dispensary unit is controlled by the medical officer of health who may in small counties or boroughs be the tuberculosis officer as well or who may have in larger counties or boroughs one or many tuberculosis officers and assistants under his direction. They are principally whole time officers who may do only tuberculosis work or perform combined duties as (a) Tuberculosis Officer and (b) School Medical Officer (or Maternity and Child Welfare Officer) and perhaps (c) Medical Officer of Health of an Urban or Rural District Council in the area. These off-

cers attend the dispensaries in the area and act as consultants to the general practitioner in carrying out home treatment particularly in the case of the insured person. The Ministry of Health have advised that patients whose treatment does not call for experience or skill beyond that which general practitioners ordinarily possess, and who are either insured persons or who can afford to pay for medical attention should not be encouraged to attend the dispensary for routine treatment. In the case of insured persons periodical reports are to be furnished to the Tuberculosis Officer by the general practitioner. It is expected however that every tuberculous person coming within the ambit of the dispensary should be entered in the register and kept under continued supervision (being seen by the Tuberculosis Officer at least once a year) until the patient (a) is considered cured, (b) had died, (c) left the district, (d) refused to continue under public medical treatment, or (e) was lost sight of.

Nurses and Health Visitors are an important part of the Dispensary Staff, (a) to assist at the Dispensary, (b) to visit the homes of notified cases reporting on social and environmental conditions to bring up contacts for examination and to follow up old patients (c) to help in after care and (d) at times do actual nursing in the homes.

The six functions of the Dispensary as set out by the Departmental Committee were:

1 Receiving house and centre of observation

2 Clearing house and centre for observation

3. Centre for curative treatment

4 Centre for examination of contacts

5 Centre for "after care"

6 Information Bureau and Educational Centre

The services available under the tuberculosis scheme are technically available for the whole community. Naturally, however, they are utilized mainly by the less well-to-do.

Under the government scheme many local authorities have prepared plans and built their own sanatoriums and hospitals, others continue to use beds provided in voluntary institutions. Many counties and boroughs use both types of institution.

The principles of sanatorium treatment we found practically the same as in Canada. It is realized that in the past there has been a tendency to underestimate the importance of rest and to start patients on graduated work at too early a stage. Dr Coutts tells us that the need for regulated occupation of mind and body as an essential part of sanatorium treatment is increasingly recognized, and that the tendency amongst thoughtful workers is to lay even more emphasis on the psychological than on the physical aspect and advantages of occupation. Occupational training has been made successful as a part of a fully organized scheme at L'apworth which is an example of a sanatorium for patients in all stages, with an industrial colony and village settlement attached, which has enabled tuberculous men to make good and re-establish themselves as wage earners living with their families.

# Disease of the Coronary Arteries Associated With Thrombo-Angiitis Obliterans of the Extremities\*

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IT is probable that the process characteristic of thrombo-angiitis obliterans involves vessels in areas other than the extremities more commonly than is believed. Such involvement may only be recognized by careful clinical and pathologic investigation. We have not had an opportunity to examine cases of thrombo-angiitis obliterans after death. Necropsy was performed in seven cases recorded in the literature. Evidence of disease of the coronary arteries was found in four. A summary of these four cases follows.

*Case reported by Buerger*—A man aged twenty-four years with thrombo-angiitis obliterans died suddenly following a Gritti-Stokes amputation of the right thigh. He had been engaged in conversation with a nurse shortly before death. The clinical diagnosis of thrombo-angiitis obliterans of the extremities was confirmed microscopically. The left coronary artery was

normal 1.5 cm from its origin, where the main branch running down to supply the left ventricle was found to be more or less filled by a fibrous yellowish-white substance which was adherent to the wall and divided the lumen of the vessel into two small parts. This fibrous process in the lumen of the vessel could be traced down only about 3 cm. The right coronary artery and veins did not appear to be changed. At the point of origin of the right coronary artery there was an atherosclerotic plaque on the right posterior sinus of Valsalva which encroached on the lumen of the orifice of the artery to such an extent as to obstruct it, in fact, the orifice was only the size of a pin-point. There were numerous pin-head and slightly larger atherosclerotic patches scattered diffusely beneath the intima. At necropsy a diagnosis was made of thrombo-angiitis obliterans, atherosclerosis of the coronary arteries, and interstitial myocarditis. The microscopic examination of the coronary

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arteries presented the typical picture of atherosclerosis

*Case reported by Buerger*—A man aged twenty-one years with thrombo-angitis obliterans of the extremities died following operation for mesenteric thrombosis. Necropsy revealed marked atheroma of the coronary vessels, the entire intima presented numerous raised patches. Here and there, however, were small button-like elevations due to nodules in the media of the vessels over which the intima appeared perfectly normal. A diagnosis was made of thrombo-angitis obliterans, extensive atherosclerosis, mild thrombosis in the aorta, celiac axis, and superior mesenteric arteries.

*Case reported by Perla*—A man aged forty-four years with thrombo-angitis obliterans had been subjected to multiple amputations because of gangrene. Following amputation of the left hand, the patient vomited twice, became cyanotic and died within a few minutes.

Necropsy revealed thrombo-angitis obliterans of the arteries of all extremities including the external iliac artery and also the left coronary. Beginning 1.5 cm from the orifice in the aorta, an organized, canalized thrombus almost completely occluded the lumen of the main left coronary artery. The process resembled that in the vessels of the extremities. The right coronary artery was normal.

*Case reported by Lemann*—A man aged fifty-five years had had obliterative vascular disease of the lower extremities for four years. Amputation of both legs had been necessary. He

died suddenly about seven hours after the onset of pain in the region of the heart and in the abdomen, vomiting, coughing, dyspnea, rapid and weak pulse, coldness of the upper extremities, low blood pressure and great pain. Examination of the coronary arteries showed them to be markedly sclerotic. There was partial occlusion of the orifice of the left coronary artery by calcareous deposits and complete occlusion of the branches of the right coronary artery by a similar process of calcification. A diagnosis was made of coronary occlusion, chronic fibrosis and calcification, chronic myocarditis and atheromatous degeneration of vessels.

In all of these cases death was apparently due to involvement of the coronary arteries. The genesis of the disease of the arteries was, however, different. In the cases described by Buerger and Lemann the disease was apparently of arteriosclerotic origin whereas in the one described by Perla the coronary arteries were involved in the process considered typical of thrombo-angitis obliterans. In Lemann's case, the sclerosis of the coronary arteries may have been only a manifestation of advanced age. This explanation does not apply to Buerger's cases as the patients were aged twenty-four and twenty-one years, respectively. In these cases three explanations present themselves: (1) thrombo-angitis obliterans of the extremities causes predisposition to sclerotic changes in the coronary arteries, (2) the disease of the coronary arteries was typical of thrombo-angitis obliterans, or (3) sclerosis of the coronary arteries and thrombo-angitis of

the peripheral arteries occurred in the same patients because they were inherently susceptible to arterial disease. The relationship of disease of the coronary and peripheral arteries, however, is an unsolved problem.

The high incidence of disease of the coronary arteries in cases of thrombo-angitis obliterans, examined after death led to our clinical study. The syndromes of thrombo-angitis obliterans and disease of the coronary arteries are incisive enough so that little doubt exists of the association of the two conditions in the cases presented.

In an unselected series of 225 cases of thrombo-angitis obliterans observed at The Mayo Clinic, there were seven in which clinical evidence of disease of the coronary arteries was present, an incidence of 3 per cent. Two of the cases have been presented previously by Brown and Allen. The age of two patients was forty years, and of the other five forty-three, forty-four, forty-five, forty-seven and forty-eight years, respectively. This percentage incidence of the association of thrombo-angitis obliterans of the extremities and disease of the coronary arteries in persons of middle age seems to us of sufficient interest to summarize.

*Case 1*—A Scotch lawyer with thrombo-angitis obliterans had been under observation since 1924 at which time he was thirty-seven years of age. A letter from his local physician stated that in January, 1926, he was called to see the patient who was found to be in collapse, semiconscious, bathed in cold perspiration and pulseless. The heart rate was 44 beats each minute. Recovery from this attack was incomplete and in about two hours from its onset a second

attack occurred. The pain was severe for twenty-four hours and he vomited twice during this time. During the week preceding he had had slight attacks of retrosternal pain opposite the second costal cartilage, radiating directly through to the back. The pain lasted only a few seconds but was associated with dizziness and a sensation of choking. After the two severe attacks described there were mild attacks lasting only a few seconds.

The patient was examined at The Mayo Clinic in April, 1926. The heart revealed only indistinct tones. The systolic blood pressure was 119 and the diastolic pressure 68, the pulse rate was 80 each minute. The electrocardiogram showed right ventricular preponderance and T-wave negativity in lead III. In December, 1927, while the patient was at home he had a severe attack but with less pain. He died in about five hours. Necropsy was not permitted.

*Case 2*—A Hebrew aged forty-seven years was examined at The Mayo Clinic in July, 1928. The history and clinical data were typically those of thrombo-angitis obliterans of the extremities. On three successive nights in January, 1926, he had been awakened with a choking sensation and severe pain across the lower anterior part of the chest, during the last attack the pain radiated down both arms. The attacks lasted three to four hours during which he vomited occasionally. Since this time definite, mild dyspnea had followed exertion. Pain occurred over the proximal heads of the clavicles and radiated down both arms with undue exertion. This was relieved by rest.

Examination of the heart, and electrocardiograms did not reveal anything of significance. The systolic blood pressure was 142 and the diastolic 90.

*Case 3*—A locomotive engineer aged forty-five years was examined at The Mayo Clinic in November, 1924. The history and clinical data were typical of thrombo-angitis obliterans of the extremities. For four years he had had distress of the chest consisting of a dull ache, present either at rest or during exercise and aggravated by movements of the chest.

the chest. Moderate exertion caused slight dyspnea. Cardiac dullness was noted 10 cm to the left of the midsternal line, the area of dullness of the arch of the aorta was 6 cm wide. The point of maximal intensity of the apex beat was in the sixth intercostal space, the sounds were of good quality, and murmurs were not present. The systolic blood pressure was 110 and the diastolic 85. The electrocardiogram, made November 27, 1924, did not show abnormalities. December 26, electrocardiograms revealed T-wave negativity in lead I. The diagnosis at this time was angina pectoris with coronary sclerosis.

*Case 4*.—A German-Irish salesman aged forty-four years came to The Mayo Clinic because of a choking sensation, and pain in the left side of the neck.

Examination disclosed thrombo-angitis obliterans of the extremities, a strongly positive Wassermann reaction in the blood, and neurologic evidence of syphilis of the central nervous system. Symptoms referable to the heart, of two years' duration, consisted of dyspnea, choking and pain in the left side of the neck on exertion, and severe palpitation of the heart. The cardiac dullness extended 13 cm to the left and 3 cm to the right of the midsternal line. The heart sounds were distant. The systolic blood pressure was 120 and the diastolic 90. Fluoroscopic examination of the chest was negative for aneurysm. Electrocardiograms revealed diphasic T-waves in leads II and III and iso-electric T-waves in lead I. The clinical diagnosis referable to the heart was angina pectoris with coronary sclerosis.

*Case 5*.—A Jewish grocer aged forty-three years was examined at The Mayo Clinic in January, 1929. The history and clinical data were typical of thrombo-angitis obliterans of the extremities. Data referable to the heart were as follows. Two years before admission the patient had experienced a sensation of pressure in the epigastrium and beneath the sternum. This distress was usually brought on by exercise after meals and was relieved by a short period of rest varying from five to fifteen minutes. Occasionally he became frightened during the attacks and perspired freely. With the most severe attacks, pain radiated

into both arms. The attacks gradually became more frequent so that three months before examination at the clinic they occurred three or four times a day.

The heart was found to be slightly enlarged and there was a soft systolic murmur at the apex. The systolic blood pressure was 130 and the diastolic 75. The electrocardiograms showed T-wave negativity in leads II and III and iso-electric T-waves in lead I. In leads II and III the T-waves had the peculiar high take-off of the so-called coronary T-waves. The clinical diagnosis referable to the heart was angina pectoris with coronary sclerosis.

*Case 6*.—A man aged forty-eight years was examined at The Mayo Clinic in May, 1928. The history and clinical data were considered typical of thrombo-angitis obliterans of the extremities. The illness referable to the heart had begun one year before admission with an attack of so-called acute indigestion lasting fifteen minutes. The pain was in the epigastrium, was very severe and associated with fear of impending death. A number of similar attacks, much less severe and supposedly due to dietary indiscretion, followed. Two weeks before admission there was sudden pain in the retrosternal region with marked dyspnea and fear of impending death. The attack had lasted one hour, but less severe attacks had occurred in which the pain radiated down both arms and into the back. The dyspnea was marked on the least exertion. The patient had to be propped up in bed.

Examination showed the heart to be moderately enlarged, there was a double second sound and gallop rhythm. The patient was dyspneic and breathing was of the Cheyne-Stokes type. Roentgenograms of the chest showed considerable infiltration of both lower hilums, the cardiac shadow was 17 cm wide. Diphasic T-waves in lead I were present on two electrocardiographic examinations. The systolic blood pressure was 158, the diastolic 100. The clinical diagnosis referable to the heart was angina pectoris with coronary sclerosis. The severe attacks of prolonged pain were suggestive of previous coronary thrombosis.

*Case 7*—A Roumanian office clerk aged forty years was examined at The Mayo Clinic in January, 1922. One year previously he had suddenly experienced a sensation of soreness and choking under the sternum followed by prolonged and productive coughing. For seven months after the first attack less severe attacks occurred irregularly. Five months before examination at the clinic he had a very severe attack of pain, with severe orthopnea and sweating. He was in bed three weeks and since then dyspnea had occurred, especially after exercise and large meals.

Examination of the heart showed an occasional premature contraction and duplication of the pulmonic second sound. Roentgenograms of the heart showed it to be 18 cm in its transverse diameter. The systolic blood pressure was 118 and the diastolic 74. Diphasic T-waves in leads I and II and inverted T-waves in lead III were shown in the electrocardiograms. The clinical diagnosis referable to the heart was paroxysmal dyspnea with coronary sclerosis.

The patient went home but returned in 1926. The symptoms complained of previously, dyspnea and cough, were still present. Edema of the lower extremities had been present for a year except when relieved by diuretics and digitalis. He was orthopneic. The cardiac dullness, as determined by percussion, extended 17 cm to the left and 5 cm to the right of the mid-sternal line. The sounds were distant and the second sound was reduplicated. The edge of the liver was felt 10 cm below the right costal margin. Moderate edema of the legs was present. The systolic blood pressure was 100 and the diastolic 80. Roent-

genograms of the chest showed the heart to be greatly enlarged. Electrocardiograms did not reveal anything of significance. The clinical diagnosis referable to the heart was myocardial degeneration of indeterminate origin, with congestive failure. Besides the symptoms and the cardiac condition, the history was considered typical of thrombo-angitis obliterans.

### COMMENT

The incidence of disease of the coronary arteries in thrombo-angitis obliterans as it occurs in our experience is probably not materially greater than the association with other diseases in the same age period. The occurrence, however, of obliterative disease of the vascular system in different situations of the body should be noted, and it seems desirable to bring emphasis to the problem so that further studies from this standpoint can be undertaken with reference to the correlation of clinical and necropsy data. It is not possible, from the material forming the basis of this study to draw any definite relationship between thrombo-angitis obliterans of the extremities and disease of the coronary arteries. Further investigation in a larger series of cases may aid materially in establishing more than a casual relationship.

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## Chronic Mucous Colitis\*

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WE fully realize when it comes to discussing a subject with the above title, that we are stepping into a severely controversial field, a field, the very definition and classification of which is open to desperate competitive argument and general lack of decision. No one condition in medicine is more confusing than the conflicting descriptions of diseases of the colon.

During the past decade, great scientific interest has been exhibited in the study of the gastro-intestinal tract, with great stress laid upon that portion proximal to the colon. In spite of this thoroughness of investigation of the upper tract, the colon has been allowed to suffer and we are still as much confused in reference to this organ, as our fathers. The very term "Colitis" is subject to many interpretations and it may be with undue optimism that we venture to discuss, even in a small way, this relatively specific complex. However, to date, in spite of the severe criticism of the term, we have encountered no substitute which would better portray to us the condition as it exists.

### ETIOLOGY

A search of the literature in refer-

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ence to an accepted etiology for this condition, yields but very vague information, and the general impression is that no determined cause has been established with any great support. According to many authorities, Nothnagel, specifically, the underlying etiology has been insisted upon as being a nervous one. Thus, in the light of present day medicine, as a causative factor for a definite organic condition, such as we are dealing with, seems questionable in accordance with reason.

From some sources we receive, as a suggestion, a condition of pre-existing constipation, which is considered sufficient. Others attribute it to the use of drugs, particularly laxatives or purgatives, over a long duration of time. Hence, the practitioner is left very much at sea in reference to any clear line of etiological thought.

A bacteriological etiology has been conscientiously sought by many investigators without definitely proven results. Several reputable workers feel that the cause is to be found in the field of bacteriology and have gone so far as to suggest specific strains of bacteria as being at fault, with the result that vaccines, either autogenous or stock, have been strenuously advocated. However, the general consensus of opinion in reference to their efficacy has proven disappointing.

## STATISTICAL DATA

The careful perusal of two hundred determined Mucous Colitis cases examined during the past several years in an urban practice (this specification of urban in contra-distinction to country practice, is advisedly mentioned) revealed the following interesting statistical data

The average age incidence was forty-one

The proportion of male to female was approximately one to four

The proportion of married to single women was two to one

Pre-existing pregnancy was seventy-five per cent

Three cases were overweight, to two underweight

Blood pressure readings revealed seventy per cent as being sub-normal

The co-incidental pathological incidence of chronic cholecystitis was thirty-seven per cent, and that of concomitant urinary infection, ten per cent. Routinely there was instituted a tetraiodophenolphthalein-dye gall bladder X-ray to determine associated gall bladder pathology

Historical evidence of previous appendectomy was twenty-three per cent

Although no figures are available, there seems to be a rather co-incidental association between colitis and visceroptosis

Eighty-five per cent of the cases presented an acute abdominal angle, that is to say the presence of less than a right angle formed by the junction of the ziphoid cartilage and the costal margins

## SYMPTOMATOLOGY

In all but a few cases, the series presented a history of disturbance of intestinal evacuation. Rather characteristically, these cases presented additional historical data, in many instances, to the effect that for no demonstrable reason they would experience relatively short periods of return to normal, or slightly loose bowel evacuation, interspersed in the course of their constipation. Cathartics of all types and descriptions, in conjunction with enemata and colonic irrigations had been resorted to for many years, as a rule, aside from medical advice.

It is to be observed, in acquiring historical data, that in the course of this self-medication experimentation, almost all patients had learned to eschew the saline cathartics, with the exception possibly, of those individuals in whom there was present a concomitant gall bladder pathology. In these latter instances the salines were preferred more for the relief of the gastric symptoms, than for the associated constipation.

It is interesting to note that a great number of patients constantly present the story that they have taken this or that laxative, specifying bran, mineral oil, fruit laxatives, apricots, prunes, raw fruits, cabbage, and such roughage vegetables, at the suggestion of friends and infrequently at the advice of physicians, in an effort to overcome the existing constipation, with the result that they themselves have observed a general increase in their presenting symptoms.

It was surprising to observe how generally unaware the average individual proved to be in reference to

their daily evacuations, particularly such common characteristics as consistency, color, bore, and other associated findings.

Additionally, in a small per cent of cases, normal evacuations once or twice daily were reported, and in spite of this history, mucous colitis was diagnosed after microscopic and macroscopic fecal examination together with physical examination. Hence, bowel regularity does not necessarily negative the presence of this suspected colonic pathology.

Abdominal pain, with few exceptions, was the constant complaint, simulating historically, the presence of various organic conditions such as, in the order of their frequency: Chronic Appendicitis, Chronic Cholecystitis, Cholelithiasis, Gastric or Duodenal Ulcer, and even female pelvic disorders.

It was noted that twenty-three per cent of the cases had been subjected to appendectomy, naturally, we presume, for acute or chronic appendicitis, with no demonstrable relief and in many instances, with the sequel of an aggravation of the previous symptoms, post-operatively. At this juncture, it might be interesting to know that in all cases of appendectomy the patient experienced a marked relief of local and systemic complaints for a greater or less period following the operation, which succeeded in buoying the general associated mental depression. However, this marked improvement was short lived, varying in length of time to a great extent with the length of hospitalization and mode of living, together with the regime that was maintained post-operatively.

The prevailing symptoms additionally, are chronic fatigue, particularly of the afternoon type, general listlessness, a rather constant daily backache, experienced in and around either or both renal regions. The presence of an associated "indigestion" exhibiting itself more particularly in gas, belching, and fullness, and often associated with the characteristic symptoms of gastric hyperacidity. Additionally, irregularity of fecal bore and consistency was commonly noted.

Universally, in those cases which had observed their bowel movement, mucus was noted, varying markedly in quantity. In several instances large quantities of yellow mucous casts have been presented by patients laboring under the impression that they were suffering from "worms" or some serious bowel trouble.

Temperature readings were generally slightly below normal, contrary to statements made by other observers. This sub-normal tendency may be attributed to the systemic condition of the presenting cases.

In all but a few cases, a distinct neurosis could readily be obtained upon historical questioning. As a rule, the mental tenor was of the depressive, rather than the exhilaratory type.

#### PHYSICAL EXAMINATION

As can be readily deduced, there are few definite consistent characteristics as far as the general system is concerned. As a rule, we encounter a greater or less degree of anemia, a definite lowering of the blood pressure, and an emotional instability is readily determined. From the pulmonary and cardiac standpoints, we have been unable to glean sufficient signs or symptoms worthy of note.

Examination of the abdomen reveals, naturally varying to a great degree, the following abnormalities

Tenderness over the entire colon, with maximum degree over the cecum and ascending colon, a lesser degree over the course of the transverse, and the least degree over the descending colon. In the mildest cases the tenderness is inclined to be absent in the descending colon, and in other cases in both the descending and transverse colon.

It is rarely noted that tenderness throughout the entire colon was absent.

Palpation of the cecum and ascending colon almost universally reveals a broadening of the cecum with very evident retention of a solid, fluid, and gas mixture. As the examining hand ascends, it encounters a rope like, lengthy mass in the course of the ascending colon, which generally elicits pain upon palpation.

Herein lies the clue to the avoidance of unnecessary appendectomies. If the examiner, suspecting the presence of chronic or acute appendicitis, will but palpate the adjoining cecum, ascending, and transverse colon, an otherwise fallacious diagnosis might be avoided. We are inclined to believe that the one common complaint in colitis cases, if no other can be commonly attributed to this disease, is that of right iliac pain, caused by cecal distention, or what is termed by some, "iliac stasis".

Digital rectal examination as a rule

reveals no additional data. Rectoscopic, proctoscopic, and even sigmoidoscopic examination in well qualified hands, fails to help us to any great degree in confirming our suspected diagnosis.

X-ray examination in conjunction with the clinician, by deduction, returns to us a confirmatory diagnosis. But specifically speaking, little help is to be obtained from this procedure, except in so far as the complete examination by X-ray of the gastro-intestinal tract, plus a barium colon enema may serve to exclude the presence of historically suspicious concomitant disease. As a rule, colonic X-ray examination reveals a general spasticity of the entire colon, or segmented portions of the colon, together with the incidence of a large percentage of ileo-cecal valve incompetence.

Blood count, together with biochemical determinations, fails to afford us any specific aid.

Basal metabolic determinations reveal only thyroidal disturbances, the incident of which in this series was only two cases, which fact differs from findings of other observers.

Stool analysis in addition to presenting the constant presence of mucous, in greater or less quantity, reveals the disturbance of intestinal flora, with the general marked diminution of the gram negative aciduric bacteria. The other stool characteristics vary directly in proportion to the existing regime. Blood, occult or microscopic, was noted in but three of the series afore-mentioned.



After a number of years of clinical experience, we have come to the conclusion that we encounter in investigating mucous colitis, many cases in which there is present, or will later be present, a pathological quartet of diagnoses

To explain more fully, the foregoing statement means that in many cases we are inclined to find two or more of the following four conditions to be present, namely Chronic Mucous Colitis, Chronic Appendicitis, Chronic Cholecystitis, and Chronic Cystitis or Pyelocystitis

In analyzing these four, it is reasonable to suppose that when one considers the embryological derivation as well as the morphological association of the appendix, that a chronic condition of the colon must of necessity, if the latter be continued over a long period of time, involve an adjacent unprotected hollow organ such as the appendix. In this relationship, it has been customary during the past several years, upon diagnosing mucous colitis, to add a diagnosis of chronic appendicitis. It is realized in making this statement, that many pathologists will take issue, particularly those who respect and restrict the diagnosis of chronic appendicitis to an entity not universally accepted.

Reasoning backward from the work of the cystoscopist, taken into conjunction with the coincidence of colitis and infections of the urinary tract, and recognizing the great prevalence of the bacteriological factor, namely, *bacillus coli*, it is again reasonable to suppose that the diseased colon is frequently the fore runner of the diseased urinary tract.

The relationship of chronic cholecystitis to the colon cannot so safely be determined, but observation teaches us that in the presence of chronic cholecystitis, the incidence of mucous colitis is extremely high, whereas the reverse is not found to be the case.

#### TREATMENT

Considerable length has been gone to in investigating the literature, authoritative or otherwise, to determine any general consensus of opinion in reference to treatment. In brief, material is exceedingly lacking and specifically vague.

The problem presented resolves itself into the care of the intestinal stasis, intestinal toxicity, gastro-intestinal discomfort, and an ever present neurosis or nervous instability.

At this juncture, it is well to call our attention to the fact that, without question, we are dealing with a neuro-gastro-intestinal cycle. By this is meant an individual in whom there is, in many instances, a basic neurosis, to which has been added a definite intestinal pathology, to which again has been added an associated neurosis of intestinal origin. In other words, we have a patient who is nervous and who is abdominally ill. The abdominal condition is capable of producing a neurosis of its own, and the pre-existing neurosis is capable of aggravating the presenting gastro-enteric condition. When we consider that we have to deal with the diseased colon which often produces reflex gastric symptoms, and additionally neurotic symptoms, we cannot help but feel that its management presents a serious therapeutic problem.

In the majority of cases, the problem set before us by the individual, is the alleviation of intestinal stasis. The different steps in its management have been subjected to great discussion, particularly in reference to dietary régime. The principle underlying the treatment of mucous colitis is to spare the bowel further irritation and to apply, through the mouth or from below, soothing remedies. In general it has been found most satisfactory through the major proportion of the management of a case, to institute, as far as possible, a diet free from roughage and raw fruit. In the very acute stages, such as are frequently encountered, in which severe colonic colic is exhibited, a fruit juice and milk diet seems most satisfactory. Our experience has been that a diet is best tolerated when readily assimilated foods, such as milk, milk mixture foods, completely and correctly pureed vegetables, avoiding those with too high a starch content, together with fruit juices, is outlined. The total caloric value to be prescribed is determined by the general condition of the case. The fat content should generally be high, depending on the tolerance of the patient. It is to be borne in mind that in those cases which present a reflex gastric hyperacidity, or a reflex duodenal irritation syndrome, care must be exercised in the selection of the individual articles of food with specific attention to the foregoing. Cognizance should be taken of possible phobias as frequently exhibited by these patients in reference to specific foods. In many instances the patient will complain of an intolerance to all foods, essentially because of the

fact that he may have exhibited such to but a single item.

Naturally, the foregoing dietary should be considered but a stepping stone toward a more normally balanced one later in the progress of the treatment.

The administration of olive oil after meals, when tolerated, is generally of value. Additionally, in many cases mineral oil, plain or medicated, orally administered, is found to be beneficial.

Almost universally, an attempt is made to change the intestinal flora by administration of a well prepared and reliable acidophilus milk, in many cases with the addition of lactose.

Routinely, oil retention enemata, of never over five ounces, of equal parts castor oil and olive oil, or mineral oil, or some vegetable oil, are administered nightly. Efforts should be made to retain the enema over night. When properly administered, most satisfactory results are obtained in provoking a voluntary bowel movement associated with a marked expulsion of flatus the following morning. Co-incidentally, it appears that the enemata tend to relax some of the colonic spasm.

At first the quantity of oil is definitely limited in view of the fact that it is anticipated that the rectum will be used in this way over an indefinite period of time and the administration of too large a quantity has proven to be an obstacle to the retention of same. As time passes the quantity is increased nightly to six to eight ounces or more.

The infrequent administration of castor oil in large dosage is indicated particularly in those cases in which there persists a tendency toward retention of mucus.

Personally, we have obtained very satisfactory results through the use of medicated colonic irrigations in the majority of cases. Contrary to prevailing opinion, we have found that when proper technic is instituted, a condition that we too seldom encounter, irrigations fulfill their therapeutic purposes. At the same time, the abuse of this helpful agency can readily produce harm in the place of benefit.

The value of establishing a daily morning or evening bowel evacuation habit, cannot be too greatly stressed in all cases.

In the use of medications, we fear, in many cases our armamentarium will be subjected to severe strain. In all cases we use belladonna in some form, principally for its anti-spasmodic results. The use of belladonna is to be noted, not as a specific for colitis, but for colonic spasm, which is an associated condition found also in many other pathological states. Experience with benzyl benzoate has proven to be gastrically disastrous when sufficient dosage is given to obtain a desired result. Ichthyol, tincture of iodine, cod liver oil, and other so-called astringents and antiseptics have proved beneficial in many cases. Furthermore, we have had what appears to be good results in the use of linseed oil or burium in small but frequent doses particularly when given in a preparation in buttermilk or in flavored gelatin.

Various hypnotics, frequently employed in the treatment with various forms of colitis, are to be highly recommended.

The diet, as a rule, is water, broth, fruit, and vegetables, particularly

of the turpentine type, the latter always administered in conjunction with the introduction of the rectal tube, are specifically indicated.

Foci of infection, pelvic disorders, particularly those presenting any mechanical contributory features should be eradicated. Caution against promiscuous operations must be entered, due to the often unfortunate post-operative effect produced on the already unstable nervous system.

Gastric analysis will often yield information, not obtainable otherwise, particularly in reference to the hydrochloric acid content which will aid in correcting the frequently associated anorexia.

Additionally, all those recommended remedial measures, such as sun baths, massage, artificial and natural heliotherapy, salt rubs, and varied systemic tonics in hypodermic or oral form, together with stomachic stimulants, for the relief of the "systemically trodden" are advised.

Finally, but not least, is the management of the co-existing or underlying neurosis, the obviation of which is by no means of minor significance. This can well be left to the field of neurology or in lieu thereof, to the qualifications of the competent internist with associated neurological aid.

As a general rule, aside from the time required for the establishment of the diagnosis with the necessary associated X-ray and laboratory tests, continued stay in the average general medico-surgical hospital tends to serve more as a detrimental influence, rather than a desirable environmental adjunct. Hence, we generally recommend proper nutrition and health resorts.

## Sicklemia

By JOSEPH LEVY, M D , *New Rochelle Hospital, New Rochelle, N Y*

THE practitioner may be faced with the patient who has recurrent paroxysms of prostration associated with low grade fever and night sweats, the pediatrician may see a child who has attacks of jaundice, growing pains and an enlarged heart, the surgeon may have an operative case whose wound refuses to close or whose abscess continues to drain. While in many people presenting such pictures, the diagnosis of tuberculosis, rheumatic fever, or syphilis usually holds, in others, all the approved criteria may be negative. The patient may then be put through many elaborate laboratory procedures to no avail, whereas a simple test may give the answer.

One only needs secure a drop of the patient's blood, place it on a cover slip and invert the slip over a glass slide, then sealing the rim with vaseline, paraffin or balsam, puts the slide aside and examine it at his leisure. Thus fresh blood can be studied over a long period of time. In a few instances one may be surprised to find the red blood cells undergoing curious changes in shape, the phenomenon of sickling occurs. This consists in the division, enucleation and fragmentation of embryonic erythrocytes in such a manner that numerous elongated, tapering, bizarre shaped red blood cells are formed.<sup>1</sup>

The symptom-complex that accompanies the sickling of the red blood cells was admirably described by Herrick in 1910.<sup>2</sup> Since then there have been an increasing number of case reports.<sup>3</sup> With reference to one hundred and fifty cases already in the literature<sup>4</sup> and the establishment of a pathological basis for the condition<sup>5</sup> one is safe in claiming this as a definite blood disease. The earlier descriptions limited the condition to the negro,<sup>6</sup> but with the study of the routine wet blood smear a similar condition was found to exist in the white race.<sup>7</sup> Because the peculiar shaped red cells are found in a symptomless people it has been claimed by many that the sickling is merely a coincidental occurrence in a more systematic disturbance.<sup>8</sup> But it has been conclusively shown that the disease has its active and latent phases and one may go into the other on little warning.<sup>9</sup> With its periods of activity, latency and recrudescences, it resembles that primary disease of the blood, pernicious anemia.

This report is based on the study of the fresh blood of 213 successive negro admissions to the New Rochelle Hospital. Twelve of these cases (5.8%) were found to have sickle cells in their blood (Table 1). Only three of these showed signs of activity. Five of the twelve had an infection of some sort. Three occurred in the course of preg-

TABLE I

Case No.	Age Yrs	Discharge Diagnosis	Hemo-globin % (Sahlb)	Red Cells Per CMM	White Cells Per CMM	Remarks on Sickling
1	M 47	Peri-rectal abscess Sickle-cell (active)	70	3,800,000	13,000	100% sickling in 16 hrs 100% reversion in 72 hrs.
2	F 19	Chronic appendicitis Sickle-cell (active)	60	3,470,000	14,000	10% sickling in 2 hrs 100% sickling in 24 hrs 50% reversion in 120 hrs 75% reversion in 65 days
3	M 25	Fracture of heel Sickle-cell (latent)	80	4,440,000	11,250	100% sickling in 48 hrs no reversion for 15 days
4	F 19	Pregnancy Sickle-cell (latent)	80	4,500,000	15,300	50% sickling in 48 hrs no reversion for 19 days
5	F 24	Peri-rectal abscess Abscess of breast Died at 26 of miliary tuberculosis Sickle-cell (latent)	74	3,800,000	8,500	100% sickling in 48 hrs reversion in 5 days

6	F	39	Chronic Salpingitis Sicklemia (latent)	85	5,000,000	7,000	75% sickling in 16 hrs reversion in 50 days
7	F	- 24	Pregnancy Sicklemia (latent)	78	4,600,000	6,200	50% sickling in 24 hrs reversion in 23 days
8	M	1/2	Phimosis Sicklemia (latent)	68	4,400,000	14,000	90% sickling in 24 hrs reversion in 19 days
9	F	21	Miscarriage Sicklemia (latent)	75	4,430,000	9,600	50% sickling in 24 hrs no reversion in 19 days
10	F	17	Acute appendicitis Sicklemia (latent)	95	5,430,000	28,000	100% sickling in 24 hrs reversion in 9 days
11	M	8	Sicklemia (active)	76	4,400,000	11,500	100% sickling in 24 hrs reversion in 48 hrs
12	F	21	Pregnancy Sicklemia (latent)	96	4,800,000	10,400	25% sickling in 24 hrs reversion in 3 days

nancy. None of the cases showed the marked anemia seen in some of the case reports<sup>10</sup>. Because of this and many similar accounts of failure to find an accompanying anemia,<sup>11</sup> the term Sicklemia is suggested in preference to such terms as sickle cell anemia,<sup>12</sup> menisocytosis,<sup>13</sup> drepanocytic anemia,<sup>14</sup> all of which have their short-comings. While it is true that the term Sicklemia is a hybrid word<sup>15</sup> it is the one that is most descriptive of the disease. Since this term was first used by Cooley and Lee, it has received much favorable comment and should displace the other misleading and less significant appellations.

*Case I*—W. B., a 37-year-old chef, was first seen on July 18, 1927, when he was admitted to the hospital complaining of a pain in the left buttock and left leg. He had no familial history of blood disease. There was a story of gonorrhea at 17, a skin eruption at 31 at which time his Wassermann was negative. His best weight was 160 pounds ten years ago, but he had lost considerable weight during the past year, weighing only 130 pounds at the present time. During this period he was troubled with constipation and because of the severe tenesmus he would permit himself to be evicted from a hotel movement for five days. During the past six months there have been frequent sweats, with fever and weakness. Pain in the left buttock, which was described as aching, had become progressively worse during the past three months. He had noticed a cream-colored discharge from the left side of the anus for the past month. His friends informed him that "his eyes were getting yellow." On examination the positive findings were a moderate anemia, a mild loss of emaciation, a temperature of 38.0°C. Temperature during the past week had ranged from 38.0°C. to 39.0°C. Hemoglobin and red blood cells were 60% and 3,800,000 respectively. The white blood cells and differential count were 13,000 with 86% pmn. Central arteries a

inguinal lymph nodes palpable. Dulness at left apex. Fissure to the left of anus one inch long discharging a purulent material. This was incised and a drain inserted. Healing was very slow, drainage persistent and he ran a low grade fever for seven weeks. There was a further incision and drainage both of the left side and an abscess that had formed in right ischio-rectal fossa. Microscopic examination of scrapings revealed a simple hemorrhagic chronic inflammation without evidence of malignancy, tuberculosis or lues. The blood Wassermann was negative. X-ray of chest showed some calcareous deposits and increased hilum shadows. The urine was acid, SG 1008, and contained a trace of albumin, no casts. Blood count on admission showed a moderate anemia of 70% (Sahli), 3,800,000 rbc. There was a low grade leukocytosis of 13,000 wbc with 86% pmn. The red blood cells sickled within twenty-four hours and reverted in three days. During his first two months in the hospital, the anemia continued, hemoglobin reaching 60% and rbc 3,000,000. Because of the slow healing and sickle cells in blood with progressive anemia, he was put on a Minot-Murphy liver diet. He improved rapidly and was discharged in two weeks, without fever and a gain of fifteen pounds. Coincidentally with his clinical improvement, there was a rise to 80% hemoglobin with 5,000,000 rbc. Three months after discharge the hemoglobin had reached 91% and the rbc 5,000,000. At this time the red cells did not sickle. Because of this marked clinical improvement and being told that his blood was normal, he stopped taking liver. He returned six weeks later feeling "tired and weak." His hemoglobin had dropped to 75% and the rbc to 3,520,000. Though only occasional sickle cells could be found in the smears, many of the red cells were indented and kidney shaped. Upon resumption of liver therapy, he was able to continue with his work and his blood count has varied between 5 and 1 1/2 million, the hemoglobin between 60 and 100% for the past year. Repeated smears during this period failed to show any sickling of the red blood cells.

*Case II*—H S, a colored maid of eighteen, was admitted to the hospital on July 7, 1927, complaining of severe pain in the back. Her acute illness began ten hours earlier with cramp-like epigastric pains which soon became generalized, persistent accompanied by vomiting. The pain finally localized in the lower lumbar regions. In addition to measles and whooping cough in childhood she has always been sickly and easily fatigued. Though she never has had any "fever", she has been troubled with "shaking chills" and night sweats for many years. Accompanying the chills she would have "rheumatic" pains in the epigastrium and left hypochondrium. Has had muscle and joint pains off and on for years. One year ago developed an ulcer over the lower part of each "shin" bone. These ulcers resisted all forms of treatment for ten months, finally healing leaving large scars. For the past two years has noted dyspnea on slight exertion and nocturia. Occasionally her sclerae would become yellow.

On examination, she was undernourished and frail. The tongue was pallid. Tonsils enlarged. Heart slightly enlarged to percussion with a rapid (120) and regular rate. Soft systolic murmur at apex which was not transmitted. There was a marked tenderness throughout the abdomen with marked rigidity of the right rectus. Because of persistent pain, marked leukocytosis (21,000) with 81% pmn and negative urine, a provisional diagnosis of acute appendicitis was made. The appendix was removed, but its pathology did not explain the severity of her symptoms. The post-operative course was marked by continuation of the lumbar and epigastric pains and low grade fever (99°F to 101°F). She developed an abscess in the incision which took two weeks to heal. She returned one year after discharge with similar complaints of fatigue, lumbar and epigastric pains and chills. She was placed on a Minot-Murphy liver diet at this time because a study of her blood revealed a moderate anemia of 60% hemoglobin with 3,470,000 rbc, 10% of which were sickled in the fresh smear. Sickling was complete in twenty-four hours. Reversion was very slow, only 50% returning to normal in five days, while 25% were still

sickled at the end of the second month. Upon her return to the clinic six months later she was free of symptoms and was able to go about her work without any difficulty. She had been eating about one-half pound of liver a day and had gained five pounds in weight. Her hemoglobin at this time was 80% with four and one-half million rbc. Sickling of cells while still present was incomplete but as in the earlier studies the sickle cells did not return to normal.

*Case XI*—L P, a colored lad of eight, was admitted to the hospital on January 24, 1928, because of severe pains in muscles of legs and arms of two weeks duration. His mother states that he has been sickly since infancy. In the first year he had rickets and during the next two years had chicken pox, measles and whooping cough. Since the age of three has been having pains in the muscles of the extremities without joint involvement, but accompanied by rise in temperature. In an effort to relieve his symptoms, a tonsillectomy was performed one year ago. Three months ago began complaining of a tired, weak feeling. During this time his mother noticed that his sclerae were of a yellow tinge and the bouts of fever and night sweats would recur every two weeks necessitating bed-care for the greater part of the time.

On examination he was a robust intelligent colored boy with an ape-like facies. The sclerae were of a greenish yellow hue. The soft palate was anemic. There was a generalized lymphadenoid hypertrophy. On admission, the heart was not enlarged but there was a soft systolic blow at the apex. The liver and spleen were both palpable about 3 cm below the costal margin, making the epigastric portion of the abdomen excessively protuberant. There were numerous scars over both tibiae but no edema. During a stay of two months in the hospital, he ran a persistent low grade fever with weekly rises to 104° remaining elevated for forty-eight hours. At the time of the elevation in temperature the spleen and liver would increase in size, there would be an increased icteric tinge to the sclerae and the urine contained bile pigments. Dur-



these episodes the child complained of severe headaches, intense muscle pains, and weakness, there was marked dyspnea, tachycardia liver tenderness and nose bleeds

He was put through an elaborate laboratory study. The tuberculin and Wassermann tests were negative. The roentgen examinations of lungs, chest, sinuses and long bones showed no pathology. The electrocardiograph showed high voltage with a tachycardia. The blood cultures were sterile. The spinal fluid was normal. A chemical examination of the blood plasma yielded Urea 28, Creatinine 0.9, Uric Acid 4.4, Chlorides 620, Sugar 87. In a fragility test hemolysis began at .44 and was complete at .32. There was an indirect Van den Bergh. The icteric index varied from 15 to 42. The urine at first was negative but showed a trace of albumin with casts on discharge. His systolic blood pressure varied from 116 to 130 mm Hg. His hemoglobin ranged from 70 to 80% and rbc varied from three and one-half to four and one-half million. During the stages of low grade fever the wbc reached a maximum of 12,500 with 60% polymorphonuclear. At no time were malaria parasites found in the smears. The red blood cells became sickle shaped very rapidly and reverted to normal within two days.

After failing to respond to various forms of medication, he was given a Minot-Murphy liver diet, and in three weeks gained twelve pounds, was free of symptoms and his hemoglobin increased to 87% with 4,000,000 rbc. Upon his return home he did not adhere to his dietary instructions and was brought back to the hospital with fever, weakness and loss of weight. His hemoglobin had dropped to 68% but there were 4,000,000 rbc. Less than 25% of the red cells sickled. He was immediately put on liver therapy, gained two pounds and was up and about in one week. The hemoglobin rose to 83% and the rbc to 5,000,000. Sickling was not complete. He has been followed in the out-patient department during the past year, and has shown no recurrence of symptoms while partaking of liver. His spleen and liver remained enlarged and the hemoglobin varied between 80 and 85%. The red blood corpuscles averaged 5,000,000, a very few of which became sickle shaped.

## DISCUSSION

From a consideration of the findings in the above cases and from the numerous reports in the literature, one observes that Sicklemia is a blood disease with symptoms and signs referable to every part of the body. The patient usually complains of being tired, weak, or easily fatigued. He may have recurrent episodes of prostration with headaches and dizziness. He runs a low grade fever with night sweats and occasionally the pyrexia may reach a very high level. He has paroxysms of jaundice with greenish yellow sclerae and bile salts in the urine. His mucous membranes are pale, his palate and tongue are pallid and the gums bleed easily. There is a generalized lymphadenoid hypertrophy. In the active stages, dyspnea and palpitation may bring the sufferer to the physician, who may find an enlarged heart, a systolic murmur at the apex and a tachycardia, all of which disappear on appropriate treatment. The gastro-intestinal symptoms of nausea, vomiting, epigastric and left hypochondriac pains may bring the subject to the operating table. The liver is enlarged, its edge tender and smooth. While the spleen is usually small<sup>16</sup> it may fluctuate in size, increasing during the active stages. Gallstones have been found.<sup>17</sup> The patient may complain of nocturia and dysuria, the urine being of low specific gravity and containing a trace of albumin. The muscle and joint pains are severe. The chronic ulcers of the leg in a young individual are of great diagnostic importance.

The laboratory findings are essential. The diagnosis rests on the pecu-

lar, bizarre, sickle shaped erythrocytes in fresh smear or in hanging drop preparations. The anemia may be moderate or marked.<sup>18</sup> The color index is usually around one, though it may occasionally fall to a very low mark.<sup>19</sup> Normoblasts may be found in the stained smear.<sup>17</sup> A leukocytosis is the rule. Some of the red cells may be phagocytized.<sup>9</sup> The icteric index is increased and there is an indirect Van den Bergh. The resistance of the red blood cells to hypotonic saline is either normal or increased thus differentiating this disease from hemolytic jaundice.

Death usually results from an intercurrent infection.<sup>20</sup> There was only one death in this series, from a miliary tuberculosis, a common finding. The splenic lesion is typical.<sup>21</sup> The spleen is small and fibrotic, with a large number of old and recent hemorrhages surrounding the malpighian corpuscles. This is due to a congenital malformation of the splenic sinuses especially about the malpighian bodies and an abnormal development of capillaries throughout these units.<sup>21</sup> The sickle shaped cells can be demonstrated in all organs. There is an increased deposit of brown iron-free pigment in the tissues, especially the liver, spleen and kidney.<sup>17</sup> Rich<sup>21</sup> has demonstrated hemosiderin in the tissues. The bone marrow shows a diminution in fat with a large number of the crescent shaped cells and hyperplasia.<sup>22</sup>

An evaluation of any particular method of treatment is difficult because of the spontaneous remissions. In the

hands of certain men splenectomy has produced results,<sup>23</sup> while others have noticed indifferent results.<sup>24</sup> Frequent small transfusions of blood have succeeded in halting the disease in a few severe cases.<sup>25</sup> The demonstration that the disease is essentially a disturbance in erythropoiesis<sup>1</sup> suggested the use of large doses of liver. The Minot-Murphy liver diet<sup>26</sup> was given to three patients. They have been followed for more than a year with a definite improvement in symptoms. Furthermore, the tendency of the cells to assume the sickle shape has considerably lessened in two and completely stopped in the other. The patients treated did not have the marked anemia seen in some of the severe cases described in the literature.<sup>20</sup> It remains for further study to determine whether liver therapy will aid in such advanced cases.

#### SUMMARY

- 1 The term Sicklemia is suggested for the symptom-complex that accompanies the sickling of the red blood cells.

- 2 Twelve cases of Sicklemia were found in a study of 213 negro patients.

- 3 Infections are a relatively common finding in this disease and are characterized by a peculiar resistance to the usual therapeutic measures.

- 4 Three active cases of the disease are described, each of which showed a marked improvement on liver therapy.

- 5 The ingestion of liver tends to inhibit the formation of sickle cells.

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# Chronic Glomerulonephritis with Hypertension and Marked Nitrogen Retention but No Eye-ground Changes\*

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**A**LMOST since the time of Bright hypertension, cardiac hypertrophy, nitrogen retention, and eye-ground changes have been recognized as nearly constant accompaniments of certain forms of chronic nephritis. Within recent years the eye-ground changes in vascular and renal disease have been particularly stressed, both from diagnostic and prognostic standpoints. Bannick<sup>1</sup> has reported severe chronic glomerulo-nephritis without hypertension, cardiac hypertrophy or retinal changes, and occasionally there have appeared case reports of advanced chronic nephritis terminating in uremia with slight or no nitrogen retention. As another variant in the picture of advanced chronic kidney disease the following case showing hypertension, cardiac hypertrophy and marked nitrogen retention but normal fundi is reported.

J H, age 43, a colored man, was admitted to the service of Dr Thomas McCrae of the Jefferson Hospital, November 12, 1928

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<sup>1</sup>BANNICK, E G. Severe Chronic Glomerulonephritis without Hypertension, Cardiac Hypertrophy or Retinal Changes, *Arch Int Med* 39 741 (May) 1927

He complained of a sense of fulness of the abdomen, headache and weakness. The patient's father died at 49 and mother at 46 from unknown cause. A sister died at 28 from heart disease. The patient had enjoyed good health until the present illness. He had frequent tonsillitis. Four years ago he had been treated for headache by a physician and told that he had high blood pressure. He had gonorrhea in 1908 but no chancre. He had been married 16 years. His wife had never been pregnant.

The present illness began in June, 1928, with an attack of hiccups followed by nausea and vomiting. Later came headache and blurring of the vision. The attacks of headache, nausea and vomiting increased in frequency and weakness became marked in October. Constipation was bothersome and likewise a bitter taste in the mouth. There had been slight loss of weight but considerable loss of strength.

Physical examination showed a robust well nourished, adult, colored man with slight dyspnea. The pulse rate was 80 with regular rhythm, the radial vessel felt slightly thickened as did the brachial and temporal vessels. The pupils were regular and reactions normal. The teeth and gums were in good condition. The tonsils were large and cryptic but there was no gross evidence of infection. Heart: there was fairly marked pulsation in the fifth left interspace outside of the mid-clavicular line. Left ventricle dullness extended 14 cm from the mid-sternal line in the fifth intercostal space. There was no evidence of enlargement of the right, nor any indication of pulmonary congestion.

There was a soft systolic murmur at the apex and at the left border of the sternum. A<sub>2</sub> was accentuated. The lungs were clear and resonant. The abdomen was held rather tensely, no masses or tenderness could be made out nor organs felt. There was no edema of the extremities.

The blood pressure on admission was 200/130. It fell to 160/100 within three days, then showed a slight temporary rise and fell again to 140/100 just before death.

The urine examinations showed a cloud of albumin and an increased number of leukocytes, occasional hyaline and many finely granular casts, but no blood. The non-protein nitrogen was 187 mg. and the creatinine 23 mg on admission. The non-protein nitrogen rose to 294 mg and the creatinine to 297 mg before death. The blood count was

hemoglobin 52%, red blood cells 3,690,000, white blood cells 8,600. The blood Wassermann was negative.

The unusual feature in this case was the result of the eye-ground examination which follows: "Right eye, media clear; disc of good color, edges sharp; vessels normal in calibre and in course. No lesions of the fundus noted. No white spots seen. Left eye, condition similar to right" (Dr S. L. Olsho).

The patient died on November 23, 1928. Partial autopsy was permitted. The kidneys were very small, the left weighed 80 gms, and the right 62 gms. They were firm in consistency, coarsely granular, and reddish-gray on section, and histologically showed the changes characteristic of advanced chronic glomerulonephritis.

# Suggestions for Effectiveness in Diagnosis

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THE science of diagnosis is by this time fairly well advanced. The physical and laboratory findings of known pathological conditions have been thoroughly worked out, are well described in numerous and excellent texts, and are efficiently taught in the schools. Methods of examining, of performing tests, of eliciting signs, have been developed to a fairly high degree of perfection. Students are systematically drilled in them, and practitioners have access to an infinite store of literature dealing with them.

Yet, with the vast accumulation of diagnostic material freely available, and with all the students systematically put through the drill in it, the relative proportion of effective diagnosticians is not as high as one might expect. There still seems to be a gap between the scientific accumulation of diagnostic information, and its application to the individual case.

Studying diagnostic methods is one thing, and solving the disease problem of the individual sick man seems to be different and far more difficult. It is frequently assumed that there is some personal factor involved, that some men are "natural" or "born" diagnosticians, and others are not. Or, again, some subtle factor of "experience" is supposed to play the essential rôle.

As a matter of fact, experience does indeed count for a great deal. The more kinds of disease conditions one has seen, the greater the range of possibilities one may have in mind to consider, and to apply to the case in hand. Perhaps there is even a definite percentage of diagnoses that cannot be made except on the basis of an unusually extensive experience. But, for the everyday purposes of the average diagnostic practice, that percentage is small. Experience is a valuable asset, but certainly not irreplaceably essential, beyond a certain minimum of fundamental requirements.

That leaves us the mysterious factor of personal gift to consider. Just as has been found to be true in so many other lines of endeavor, I have a strong suspicion that in diagnostic work, the personal gift consists of a personal willingness to put in a lot of hard work digging out the subject thoroughly and systematically. In that respect, *diagnosis* does not differ from any other human job: the fellow who works hardest at it gets the farthest in it.

"Thoroughly"—that is the key to the secret. Perhaps occasionally it is possible to look across the room at a patient and make a brilliant diagnosis. I find such opportunities exceedingly rare; which is fortunate, for such a

practice is dangerous. Certainly that procedure is of no use in obscure cases, such as constitute the majority of the work of a man in the diagnostic specialty. When the word "thoroughly" is taken literally, it means a great deal. It is much more easily said than done.

I have seen medical men look at a patient's chest and pronounce it "negative" or "normal." I have taken that same patient on the same day and spent an hour or two on him, and filled a page with notations of the pathology I saw in his chest. Why does one man see nothing and another find a long list of signs? Certainly they are there, in plain sight. After they are pointed out to the first man he readily admits their existence. Certainly the knowledge is not esoteric or recondite. It is found in every textbook.

The reason is that pathologic findings are not evident to the casual glance. There is no "X" marking the spot with an arrow pointing to it. If the examiner looks at the chest as a whole and taps on it a little, hoping that he may stumble across something he doesn't know just exactly what, the chances are that his report will be "negative." *The examiner must look for definite items.* If you take a general glance at a room, and someone asks you the next day whether or not a radio console was present, you will not know. But, if while you are looking at the room you look around definitely for a radio console and check whether or not it is present, then you will know definitely.

It is necessary when making an examination, to have in mind a series of

concrete items. The presence or absence of each one, its variation from the normal and the amount of that variation, must be checked, one by one. What these particular items may be is not part of this paper. They are in the text-books, and belong to the science, not the art of diagnosis.

However, continuing to use the chest as an instance, we may illustrate. In the chest I check over forty-eight concrete physical items before I consider that I have made a proper examination.

- The tension and size of the various muscles of the shoulder-girdle;
- The angle and prominence of the clavicle,
- The width of the area of hilum dullness,
- The degree of expansion of each quadrant;
- The expansion rhythm of each quadrant, front and back,
- Etc, etc

These are taken up in systematic order, one by one. While each item is being investigated, the mind is concentrated on it to the total exclusion of all other considerations; and then the next one in order is taken up in the same exclusive way. There can be no skipping about, no sketching over two or three things at one time. Once the job is started it must be carried straight through, no matter whether the first findings are normal or pathognomonic. Otherwise the procedure has no value, and need not even be begun.

Only when a complete catalog of clinical findings has been accumulated by going over the patient in a systematic way, investigating them one at a

time, and making careful written records of them, is the examination of any diagnostic value. The study of such a record is the only thing that can form a dependable basis for a safe and correct diagnostic reasoning process.

In other words, a correct diagnosis depends on the possession of all the informational data in the problem. One missing item may cause a total reversal of the reasoning process and result in a wrong diagnosis or a failure of diagnosis. Diagnostic errors are in most cases the result, not of the inability to reason from clinical evidence, but of the *failure to find it* because of the lack of thoroughness.

"Thoroughness" is a word much misunderstood. In diagnostic work it signifies the analysis of a problem, such as a chest examination, into its component details, the arrangement of these details into a systematic schedule, and the accurate following of this schedule in order and without omissions. Thus and only thus can diagnostic problems in general be solved.

Now, it is conceivable that a medical man after many years of wide and vast experience in a given line of diagnostic work, will be able to keep such a schedule of details in his mind and work from it by memory. But this feat is impossible to most of us ordinary mortals. There are a thousand obstacles to working from memory. If the examiner could isolate himself and his patient on a desert island and have a week's free time for his examination, he might perhaps be justified in depending on his memory. But, in a busy office on a busy day, the telephone, the patient's conversation gets

him off the track in taking the history; in making the examination, an unexpected finding will make him forget his plans, in any kind of diagnostic routine, extraneous interruptions are always coming up. Only after the patient has left the office, do we suddenly realize that we have omitted some essential point, and the result is a flaw in the diagnosis.

The schedule for the examination procedure must be down on paper. Only by means of a detailed written or printed list of the items of history or examination procedure is it possible to adhere to system and accomplish the requisite thoroughness, and at the same time get away with a reasonable volume of work in this busy world. The examiner should either have a schedule card to follow, or preferably a blank to fill out. If he has such a blank containing every item of information that he requires in history, examination, and laboratory, and if he goes through it faithfully, step by step, before he lets his patient go away, his examination will be "thorough." In no other way is it possible to avoid missing essential evidence.

Of course it is tedious. Of course it is hard work. It confirms our previous hazard that success in diagnosis is not a gift, but a willingness to dig. Correct clinical diagnosis depends far more on getting *all* of the clinical information and not missing anything, than on any exceptional ability or brilliance. And the getting of this information is hard work.

Once I was involved in a medico-legal case in which a man was suing his employer, claiming that he had been injured in the spine. A history



of the accident did not seem to warrant such a conclusion. The insurance company retained a brilliant internist to testify in its behalf, and this internist had a "hunch" that there was some sort of a diffuse lesion of the central nervous system. He kept thinking of syphilis. I was called in to testify that syphilis was not present as far as clinical and laboratory evidence indicated. In my blind following of routine, I found the blood-picture of a pernicious anemia, and the patient's spinal-cord symptoms were at once explained. The other man had merely neglected a detail.

The human mind is fallible. It is prone to neglect detail. Therefore we dare not depend on the human mind to keep track of detail. Some mechanical system for taking care of detail must relieve the mind of such responsibility.

The particular items on the examination schedule will vary with the individual examinee, and with the purpose for which the examination is being made. In making up a routine list of signs and symptoms to use for this purpose, it is well to remember that it is better to have too much diagnostic evidence, than not enough. Most of our diagnoses are verdicts rendered on the basis of circumstantial evidence, and it is well to have an excess of confirmatory evidence. The schedule of these signs should be se-

lected and arranged after a thorough preparatory study of the particular subject, such as the chest, or the kidney, for which it is being arranged.

When the worker has once selected and arranged his schedule, he ought to follow it rigidly, consistently, always in the same order. Only after considerable practice with it, can he use it as an efficient tool. When he does get used to it and learns what it will do, he will find that besides increasing his scientific accuracy, it will enable him to do a larger amount of examination work in a shorter time, with less fatigue and less mental strain. Working extemporaneously or from memory, is an exhausting job.

By way of illustration, I append a blank which is used in this office for chest examinations. Similar blanks are used for the abdomen, for heart and kidney function, etc., comprising a total of nineteen different diagnostic blanks. The blank is so arranged that a minimum of writing is required during the making of the examination. Findings are listed in all possibilities on the blank, and the record is made by x's, check marks, zeros, and crossing out words. To facilitate future reference, a summary sheet is included in the history after the work is completed, reviewing all significant findings. The mimeograph process is used for these blanks as being less expensive than printing.

Breuer, D-1, Pulmonary

Name

Date

Case number

#### DIAGNOSIS

Tuberculosis, pulmonary

apex, hilus, generalized, left, right, dry, moist, infiltrative, exudative, cavities, primary, secondary

chronic, acute, slight, moderate, severe, active, healed,

*Front*

	right	left
Type average, long narrow, flat pigeon		
Enlarged venules in skin		
Hilus dimple		
Shoulder drop (pt rt lft handed)		
Clavicle prominent		
Clavicle horizontal, angle, increased		
Head tilt		
Muscles (S)pasm, (A)trophy, (H)ypertrophy ..		
Sterno-mastoid		
Scalenes		
Trapezius (concave crest)		
Deltoid (pointed shoulder)		
Pectoralis major (flat chest)		
Intercostals, upper, lower		
Skin and tissue turgor apices		
Skin sensation (I)ncreased, (D)ecreased		
Vasomotor skin reaction red white		
Tactile fremitus		
Rales, apices		
Rales, axillae		
Expansion apices		
Expansion bases		
Lagging, apex		
Percussion resonance, apices (H, P, D, T)		
axillae		
Increase of resonance in inspiration, apex		
Vocal pectoriloquy (location)		
Whispered pectoriloquy, (location)		
Breath sounds, apices (R, F, C-W, T, P-E)		
axillae		

*Back*

Muscles		
Trapezius, upper, middle, lower		
Rhomboids (wing scapula)		
Scapular border		
Percussion resonance, suprascapular		
middle (interscapular)		
bases		
Tidal excursion		
Kroenig's isthmus		
Breath sounds, suprascapular		
interscapular		
bases		
Lagging scapula		
Rales, suprascapular		
interscapular		
bases		
D'Espine's sign to	D vertebral spine	
Stoop shoulders		
Scoliosis, kyphosis, lordosis, rt, left.		D L

## SUMMARY

Infectious

Reflex

Local

X-Ray

Environmental factors

Psychic factors

# Dental Infection

By A G SCHNACK, A M, M D, *Honolulu, Hawaii*

THE subject of focal infection, especially with regard to dental infection, still holds the lively interest of both medical and dental professions. Vitamin deficiency as a basic cause for numerous of our pathological dental conditions has stimulated new interest in this field and new conceptions have perhaps resulted. Our theories of vitamin activity are constantly undergoing alteration, as new facts seem to become established. My aim here is to briefly sketch some of these newer ideas in their relationship to dental infection, and perhaps show how they apply in a medical way. The vastness of the material will not allow us to dwell on any particular phase of the subject. Dental hygiene has assumed a rôle of greater and greater importance as our knowledge has advanced. It has resolved itself into pre-eruptive and post-eruptive care of teeth. The pre-eruptive care of teeth has more recently been shown to have a profound effect on their future condition. A host of investigators are enthusiastically at work on the effects of vitamins on the structure and subsequent welfare of teeth. Vitamin A, the antixerophthalmic vitamin, has been thought by some to have a definite effect on growth, physical vigor and possibly resistance to infection. The lack of Vitamin C (antiscorbutic vitamin) has a pronounced

effect on the calcification of the teeth of some animals but this does not seem to apply in the case of humans. Much still remains to be proven. Vitamin D, an antirachitic vitamin, is most necessary in bone and tooth development. Hypoplastic tooth development with deficient calcium deposit is frequently the result of either vitamin deficiency or acute or chronic illness. The question of the calcium of the blood as a necessary factor in the development of bony and dental tissue has been most elaborately investigated, some investigators<sup>1</sup> claiming a great difference in the availability of calcium for tissue use, depending upon whether or not the calcium is in ionized or unionized form, diffusible or non-diffusible, the former being claimed to be all important in calcium metabolism. The relationship of sunlight to the production of this diffusible or available calcium is perhaps important. Numerous investigators have shown that substances like cod-liver oil, especially after exposure to direct sunlight or certain of the ultra-violet rays are capable of preventing or curing rickets in humans and animals. Milk from mother or other sources is apparently not capable of curing or preventing rickets unless the individual or animal furnishing the milk receives an adequate exposure to actinic rays. The actinic ray itself is again directly

capable of preventing or curing rickets. It is thought that perhaps the cholesterol of the blood, which becomes very strongly antirachitic by exposure to sunlight, absorbs sufficient actinic ray for this purpose through the skin. Ergosterol, a body sterol, after activation by actinic ray, has very powerful antirachitic properties. It may be of interest to note that the exact nature of the antirachitic factor has never been proven. It has been spoken of as "stored radiant energy" and thought that cod-liver oil, cholesterol, ergosterol, are merely vehicles of this energy. Dietary and vitamin deficiencies play an important rôle during the formative stages of teeth, and these dietary measures or corrections should be instituted early in pregnancy, as some of the teeth begin development as early as the forty-second day. Anything that induces a faulty development of teeth may be looked upon as a primary predisposing cause of caries. We may have enamel pits, or crevices, enamel lamellae<sup>2</sup> and other irregular areas of deficient calcification and faulty enamel structure, mottling, malocclusions and impactions with improper contacts, all predisposing to caries. It may be mentioned that different illnesses produce characteristic dental abnormalities, and that the presence of enamel pits and differences in enamel mottling might be used for the differential diagnosis of diseases during the formative and eruptive stages of dental development. The endocrine glands, especially the parathyroids and pituitary body, have definite direct and indirect effects on the growth of skeletal structures and teeth, and on general calcium metabolism.

After the tooth erupts, exposure to the oral juices, which may be modified by bacterial and chemical action and systemic diseases, often results in caries, the forerunner of most of our dental infection. As stated above the pre-eruptive care of the teeth will have a very important bearing on the course of post-eruptive events. The deciduous teeth when diseased often have some influence on the oncoming permanent set although we often see good permanent teeth following very badly developed and decayed deciduous teeth. It is generally conceded that enamel, after eruption, does not alter its calcium content, although possibly by a process of dehydration, may harden still further. It may be mentioned however that this viewpoint is not universal, some contend that variation in lime content occurs. While the outermost enamel layer is undoubtedly sealed from oral juices, there are minute enamel channels increasing in number as they approach the marginal tufts and plexuses, which communicate freely with the dentinal tubules and pulp. Osmosis and diffusion, it seems, should play some part in the dental lime metabolism. Osseous tissue may lose much of its lime content especially with disuse and conditions are not so very different with dentine and enamel. It has been thought that the salivary juices have qualities imparted by vitamin rich diets which prevent caries. The degree of salivation has some bearing on the process of dental decay. In illness a lessened flow of saliva often favors the development of caries. Although it is inconceivable that active mastication could alter the dental enamel, such

jaw activity is thought to improve the general oral state and tend to the prevention of caries. Coarse foodstuffs, aside from any possible vitamin action, have a decided value. It is said that northern Scotsmen who eat a great deal of coarse bread generally have good teeth while their brothers in the lowlands eat most of their cereal in pap form and have much caries. A cow fed on soft food and not allowed to graze will soon lose its front teeth, according to dental authorities, the process resembling ordinary pyorrhoea of humans. Whether active mastication benefits by toning up the general oral condition, or by increasing salivary flow, or by mechanically cleansing the teeth, is difficult to state, but benefits do accrue. Animal experimentation seems to indicate that most cereals contain an anticalcifying agent, which may however be combatted by antirachitic agents in diet and sunshine.

It is fairly well established that certain salivary conditions favor the establishment of caries-producing organisms (acidifiers) amongst which is the *Bacillus acidophilus*.<sup>3</sup> There seems to be some question as to whether the decalcification proceeds in the interprismatic substance or whether the enamel rods first decalcify, but the production of acid products, especially lactic acid, is apparently the chief cause of lime salt absorption. It has been suggested that antiperistalsis in the esophagus during sleeping hours may regurgitate gastric acid into the mouth. With slowly advancing caries the dentinal tubules are frequently sealed by the deposit of secondary dentine as the infection advances toward the pulp chamber, and the pulp cham-

ber often shows evidence of secondary dentine deposit, this is also frequently seen when the irritation is due to thermal stimuli through deep metallic fillings or to mechanical and chemical stimuli. With the pulp chamber once involved in infection our medical problem really begins in earnest. During the early stages of pulpitis we may have a great deal of pain (toothache). These neuralgic pains may produce numerous secondary phenomena, such as, headaches, pains over the distribution of the trigeminal sensory nerves, general nervous irritability and debility, facial tics, gastro-intestinal upsets etc. It is quite conceivable, if one admits such a thing as focal infection, that a pulpitis could easily be the starting point for other systemic infections. The apical dentinal tubules communicate freely with the cemental tubules and these in turn communicate freely through the pericemental membrane with the alveolar Haversian system. One must be impressed by the great difficulty of introducing sufficiently strong and diffusible antiseptics to sterilize the pulp chamber and its innumerable lateral and peri-apical communications. The resulting peri-apical infection depends not so much upon the number of bacteria reaching this area as upon the ability of the body to react and hold in check the offending organism. The reaction of the lung to invasion by the tubercle bacillus has probably been studied more in detail under varying conditions than any other kind of infection of long standing, and the fact that most dental infections are also of a more or less chronic nature offers us a good comparison for the sequence of events. The reaction to infection

about a tooth apex, like tuberculous lung infection, depends in great part on the allergic response or hypersensitivity of the individual to the invading organism at the time the infection occurs. With marked hypersensitivity present we expect to find a considerable peri-apical inflammatory reaction. In the very early stages bony changes have not had an opportunity to appear, and mere exudate through the peri-apical region may not manifest itself on the radiograph. No surgeon expects to find any marked bony changes in a radiograph of an acute osteomyelitic condition in the very early stages. Peri-apical osteomyelitis or apical abscess gradually produces osseous changes the character of which depends in great measure upon the exudative reaction. It would seem that osseous necrosis and solution results in great part from asphyxiation and local pressure in the peri-apical structures. The greater the exudate the more of these features one would expect. It is well-known that an apical abscess which establishes drainage through a sinus (gum-boil) or through the pulp chamber soon loses much of its identity. New osseous tissue soon forms within the abscess area and except for a slight disarrangement and thickening of the cancellous structure nothing abnormal may be made out in the dental radiograph. With long persisting abscess, especially where no drainage has been established we are more apt to find a certain amount of cementum absorption, often associated with a hypercementosis of the cementum adjacent to the infection area. The abscess itself in its acute stages shows no line of demarcation, but after awhile becomes walled off by a

fibrous sac often showing an epithelial lining, both elements being derived from the pericemental membrane; the epithelial lining being derived from the epithelial cords, embryonal structures, remnants of which are always present in the pericementum. This fibrous sac constitutes a so-called granuloma and frequently adheres to the tooth apex upon extracting the tooth. The sac may contain debris, dissolved cells, and usually gives positive bacterial cultures. A thin outer lime wall may still further isolate such a sac from the alveolar structures and its is often questionable whether such a process could in any way be a starting point of systemic infection. We frequently find a less violent peri-apical inflammatory process, evidenced by a slight turbidity about the tooth apex and a thickening of the peri-apical bony structure. This area may be small or may be quite large in some cases extending to the main nerve canal and causing severe neuralgic pains extending over the area of the nerve distribution. The extraction of a so-called abscessed tooth results in the absorption of considerable of the alveolar crest, and the abscess area and the root socket are filled in with bony tissue to a certain degree. After this process has completed itself we soon find evidence of other bony changes, the bony cancelli which were previously thickened from infection now thin out once more. The result is a bony structure practically identical with the surrounding normal bony structure. The normal stresses and strains on the jaw bone brought about by the muscles of mastication are responsible for the arrangement of the bone cancellations which are fashioned to best resist such

stresses Should the site of a tooth previously extracted remain turbid and show disarranged cancellous structure it is thought to probably indicate that there is a residuum of infection, as new bone does not develop normally in the presence of infection or other irritants Pyorrhoea (alveoloclasia) has received considerable attention and opinion is so varied and unsettled that one must tread lightly or come in for criticism for being dogmatic The underlying cause for this condition has not been settled We find a certain amount of alveoloclasia in practically every adult beyond middle age In many cases it might be termed senile atrophy Local oral conditions such as subgingival tartar deposits, trauma, etc., are thought to be at least contributory causes It seems to be, in many cases, accompanying systemic states, such as anemias of long duration, chronic illnesses, etc The microscopic picture showing extensive infiltrations with inflammatory products in the gingival tissue, the absorption of the alveolar crest, and indipping of the squamous epithelium, show the process to be truly inflammatory The fact of open drainage into the mouth of most of this material, makes one hesitate in placing too much emphasis on this, except in extreme cases, as a starting point of systemic infection and symptoms Unless the radiograph shows a somewhat walled-off lateral abscess, we have not quite the amount of assurance in hoping for cures from tooth extraction as we have when we view apical abscesses The question of focal infection whether from sinuses, tonsils, teeth, gall-bladder appendicitis, etc., has been pretty definitely settled as fact The specificity

of location of infection in the body is unquestionably so, at least with regard to certain organisms As a common example of this, undoubtedly proven, is the frequent involvement of heart muscle and valves and joints with streptococcus infection of throat<sup>4</sup> So we may feel that other organisms develop easiest at certain sites in the body, perhaps tissue reaction being in great part responsible The work of Rosenow, Meisser, and others in animal experimentation is too well known to need repetition The mere presence of a focal infection may through immunization protect the patient against infection elsewhere in the body, but let the body resistance decline from causes such as nervous worry, over-work, exposure to cold, starvation, and diseases of various kinds, and the individual again runs a risk of systemic infection A traumatized joint, or a joint exposed to cold may not be painful until we have the superimposed toxins from a dental infection A person must be in good physical condition to take care of focal infection, but even then he may not escape, as immunity is not entirely a problem of keeping physically fit The question often arising before one is the question of tooth extraction We are confronted with the problem of running the risk of future infection by retaining any pulpless tooth, and again our patient may suffer no ill effects from retaining a few harmless-looking devitalized teeth The familial tendency to certain kinds of disease is of course an important consideration The loss of teeth may well be balanced by the chances one takes in retaining them Our commonest cause today for the careful investigation of teeth from the



purely medical point of view is the variable symptoms complex of arthritis and neuritis, and possibly myositis, bursitis and tendinitis. Every ache or pain is thought by some to have its origin in the teeth. While the supposition may be erroneous, it does good in bringing the patient into more frequent contact with his dentist. A difference in viewpoint in regard to the nature of these aches and pains is held by many. That there is an actual lodging of bacteria in joints, nerve sheaths, bursae, muscle tissue, etc., is no doubt occasionally the case, but not the rule. No one would expect a true bacterial arthritis to clear up in a day or so after the removal of an abscessed tooth. Rosenow and others explain arthritis and neuritis and such symptoms as due in great part to circulation of strong bacterial toxins which have a predilection for the affected tissue. Some of these toxins may be extremely powerful. When we consider the toxicodendrols of poison ivy, for example, we feel more in harmony with such ideas. I personally think that some of our quick results obtained by tooth extraction can be best explained on the basis of non-specific or specific protein therapy "protein shock", the protein whether bacterial or body protein absorbed into the circulation through the macerated root socket being sufficient to cause a body reaction which might eliminate the symptoms for a shorter or longer period. One might say that the temporary flare-up was due to increased toxin absorption, which is probably often so, but it seems in some cases not to matter which tooth was extracted, as a temporary reaction with subsequent benefit is occasionally seen

after removal of a healthy tooth by mistake. Psychology cannot explain all such results. Orthopedic methods for relieving arthritis symptoms, such as wearing a high plaster of Paris collar for cervical arthritis, and braces for lumbar and sacro-iliac pains, make one hesitate in proposing the exact etiology of these pains. Mechanical trauma apparently accentuates the irritated condition of a painful joint. Our mechanical appliance may lessen trauma and prevent joint movement and painful joint surfaces may be separated by stretching. Breaking down of muscle spasm about a painful joint by such methods would also lessen pain on movement. Joint swelling is necessarily a vascular phenomenon, the result of irritated vascular nerve terminals rather than a direct effect on synovial surfaces. An acute antrum (Higmore) will often be accompanied by neck stiffness and a pain running through the occipital region of the head. We know of no direct or indirect nerve connection to throw the cervical muscles into spasm and we must fall back on the circulating toxin idea or an indirect nerve stimulation (sort of overflow phenomenon) to explain events. Likewise pulpitis or apical abscess may give a painful stiff neck and pains may be felt at the terminations of the nerves arising from these cervical segments. It is well-known that a continuous toothache will stimulate the entire nervous system until what seems to be a trivial pain at first may become intolerable. Any slight deviation from the normal at other points, under ordinary circumstances of no significance, will now produce symptoms of importance. Nerves become frayed. Gastric symp-

toms develop. The meal ordinarily easily handled lies idly in the stomach for hours overtime and one's appetite is lost. The more one studies pathological dental conditions the more reason there seems to be to link many systemic conditions with these focal infections, although we still find many orthopedists who, because of the results they often obtain with their mechanical appliances, take a very conservative view of such infection. The patient's condition may not warrant the wholesale extraction of merely doubtful teeth, as the shock of such operations may be quite serious and even fatal. Today, as in other branches of medicine, preventive dentistry is assuming greater importance. This consists in caring for the deciduous and permanent teeth both in their pre-eruptive and post-eruptive state, by a dietary regimen, oral cleanliness, vigorous exercise of jaws and teeth, and attention to early caries, often best determined with the aid of the radiograph. What today seem to be hereditary faulty teeth may prove to be due to familial tendencies to avoiding certain foodstuffs, or tendencies to faulty hygiene and poor living conditions, or exposure to chronic diseases. Many are coming back to the old-fashioned idea of the importance of the action of "sweets" on the teeth. Candy before bed-time without thor-

ough cleansing of teeth and mouth before retiring will produce conditions favoring the formation of lactic acid. During sleep the flow of saliva is greatly diminished and stagnation and concentration of deleterious oral products is the rule. Large amounts of candy seem to be directly responsible for dental caries, in many cases, perhaps often being superimposed on faulty dental development. Deciduous teeth are more vulnerable than the permanent set, and often present the appearance of massive decay. M. R. Jones working in our laboratory has coined the term "odontoclasia" to describe this massive decay of enamel and dentine, and will soon publish results to show that sunshine, at least in the large amounts we get it here, is not the all important factor in proper dental calcification. The problem, considered by some to be a "cut and dried" proposition depending upon the relationship of anticalcifying agents, vitamin D, and sunlight, is still apparently unsettled.<sup>5</sup> The rôle of phosphorus in dental metabolism is another unsolved problem. One can hardly make a statement with regard to anything mentioned here without finding much difference of opinion. Much of the animal experimental work has given results which do not seem to apply satisfactorily to humans but time may eliminate the discrepancies.

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## Editorials

### THE PASSING OF THE NOGUCHI ORGANISM OF YELLOW FEVER

In an article written in 1927 by Noguchi for Cecil's Textbook of Medicine he states that yellow fever is caused by a specific micro-organism, *Leptospira icteroides*, first isolated in 1918, during an epidemic of yellow fever in Quayaquil, Ecuador. The organism is present in the circulating blood of the patient at least during the first three or four days of the illness, and is occasionally found in the liver or kidney at autopsy when the patient had died early in the disease. It can be isolated either from the blood of yellow fever patients during the febrile stage, or from the blood, liver or kidneys of animals experimentally infected with the blood of yellow fever patients. It is present in such small numbers in the peripheral blood that its direct detection microscopically is extremely difficult and its transmission to animals inconstant. It has been shown that virulent leptospiras are present in the bodies of *Aedes* mosquitoes which have been allowed to feed on yellow fever patients or experimentally infected animals. The blood serum of yellow fever convalescents gives specific immunity reactions (Pfeiffer phenomenon, agglutination) with *Leptospira icteroides*. The pathological changes in yellow fever are due to direct invasion by *Leptospira icteroides* of certain visceral or-

gans for which the organism exhibits a special preference. The character and distribution of the lesions produced in susceptible animals by means of pure cultures of *Leptospira icteroides* are practically identical with those of human yellow fever. Convalescent serum from yellow fever gives a positive Pfeiffer reaction with *Leptospira icteroides*, but not with *Leptospira icterohæmorrhagiae*, the causative agent of infectious jaundice, and vice versa, this mode of differentiation has been used in some tropical districts where cases occurred which might be either yellow fever or infectious jaundice. The specific treatment consists in the early administration of anti-icteroides immune serum in sufficient quantity. This is a polyvalent anti-serum prepared by injecting cultures of *Leptospira icteroides* into horses. It has been used in about 150 cases, with reduction of the mortality from the usual 50 or 60 per cent to 10 to 15 per cent. Prophylactic vaccination offers another means of preventing yellow fever, and consists in the inoculation of a killed culture of *Leptospira icteroides*. The development of immunity requires a period of 10-15 days, and the duration of protection is probably not longer than 5 or 6 months. Comparison of case incidence among vaccinated and unvaccinated persons during epidemics of yellow fever in Ecuador, Mexico, Guatemala and northern Peru has shown that vaccination confers protection against the

disease in the majority of instances. More recent investigations in Mexico, Peru and Brazil have confirmed the etiologic relationship of *L. icteroides* to yellow fever. The above represents Noguchi's claims for his organism that the *Leptospira icteroides* is the etiologic factor in the production of yellow fever, that it occurs in the Aedes mosquito, that it produces in experimental animals an identical pathology of that of human yellow fever, that the blood-serum of yellow fever convalescents gives specific immune reactions with this organism; that the specific treatment of yellow fever consists in the early administration of a polyvalent antiserum prepared by the injection of horses with cultures of *L. icteroides*, and that prophylactic vaccination by the inoculation of killed cultures of this organism confers protection against the disease in the majority of instances. If these claims made by Noguchi for his organism were true it meant that the problem of yellow fever was conclusively settled and that this disease could in the future be controlled successfully, another great victory for the modern research laboratory. Unfortunately there were too many weak spots in Noguchi's claims, that in spite of the influence of his name and associations led to doubt among many workers, particularly the Cuban group, Agramonte, Guiteras, Lebrede and others. Noguchi's claim did not fit the epidemiological facts, and, it was soon discovered, neither the serological nor the pathological. *Leptospira* did not conform to what must necessarily be characteristic of the yellow fever parasite, in view of the former's almost saprophytic character. The cul-

tural characteristics of the organism and the lesions produced by it in experimental animals seemed to the Cuban workers to be like those of *Leptospira icterohaemorrhagiae* of Weil's disease. *Leptospira icteroides* seemed to be infective upon lower animals in almost every way rather than through the mosquito, while we know that yellow fever is not transmissible in nature by any other way than through the mosquito. In yellow fever the virus is not present in the blood after the third or fourth day, while in Weil's disease, *L. icterohaemorrhagiae* is best obtained by injecting a large quantity of the patient's blood into guinea-pigs even as late as the eighth or ninth day of the disease, in this way resembling *L. icteroides*. In 1924, Agramonte stated that the serologic differences between *L. icteroides* and *L. icterohaemorrhagiae* are not pronounced, in fact they are no greater than those we find between organisms that form part of the same group. This question was definitely settled by the work of Selkards and Theiler, who showed that an absolute interrelationship exists between the two organisms, the serum of *L. icterohaemorrhagiae* causing positive Pfeiffer reaction upon *L. icteroides*, and vice versa. The culture of *icteroides* used for these experiments was furnished by Noguchi. Under the conditions of their experiments these workers found no differences between the two leptospira. Other investigators, Gray, Carnal, Aitken Smith, etc. obtained negative Pfeiffer reaction upon *L. icteroides*, using yellow fever convalescent serum. The same result was obtained with the yellow fever convalescent serum at Paraty, Brazil, which serum gave no protection

against either *L. icteroides* or *L. icterohaemorrhagiae*. In a paper read at the New Orleans meeting of the College, Agramonte summed up the situation by saying: 'The etiologic agent of yellow fever has not yet been demonstrated, that the claims of Noguchi and his disciples for *L. icteroides* on the specific germ of yellow fever have been conclusively disproved, because *L. icteroides* and *L. icterohaemorrhagiae* show crossed serologic reactions indicating their identity, and that yellow fever convalescent serum does not protect against *L. icteroides*, while serum from convalescents of Weil's disease does protect against both *L. icteroides* and *L. icterohaemorrhagiae*. Further, *L. icteroides* gradually increases in numbers in the blood of inoculated animals, while the real yellow fever germ disappears from the circulating blood at the third or fourth day *L. icteroides* fails to infect mosquitoes so that in due time the latter may infect man. Finally, *L. icteroides* is able to penetrate the unbroken skin and produce infections, while yellow fever has been shown to be non-contagious, even through cuts or abrasions of the skin. Agramonte concludes therefore, that any vaccine or serum prepared with *L. icteroides* can have no value either protective or curative as regards yellow fever. As regards the character of the pathologic lesions caused by *L. icteroides* in experimental animals, Hoffman regarded the changes found as typical of Weil's disease in man. Wandstrom found the changes in the experimental *L. icteroides* animals to be not as severe or as marked as has been reported in human yellow fever cases, and as not differing in type from those of experimental infectious jaun-

dice. According to Klotz, the virus of yellow fever in West Africa has not been demonstrated, although the effort has been made by a number of investigators to isolate the *L. icteroides* by the Noguchi technique. 'The quality and distribution of the lesions arising in West African yellow fever are the same as that in America, and we are justified in concluding that they are one and the same disease, but the most careful search of the autopsy cases failed to demonstrate the presence of the Noguchi organism. Many attempts were made to infect guinea-pigs, but these were all negative. Inoculations into *Macacus rhesus* monkeys were made by Stokes and Bauer with the first demonstration of successful transference of yellow fever to a highly susceptible animal and its subsequent retransfer to new animals by inoculation and the mosquito. The gross and microscopical pathology of the tissues in these animals showed all the characteristic lesions as have been described in man. The results obtained by the West African workers, thoroughly negative as regards the Noguchi organism, must be considered the final death-blow to Noguchi's work and claims for the *Leptospira icteroides* as the etiological factor of yellow fever. The identity of this organism with *Leptospira icterohaemorrhagiae* must be accepted as proved. The etiological problem of yellow fever remains, therefore, still unsolved. For its solution we must turn to West Africa, the last stronghold of this disease, where the first successful transmission of yellow fever to an animal with resultant pathologic lesions as seen in human yellow fever arouses hope as to the final solution of this etiological problem.

## Abstracts

*Pulmonary Abscess and Pulmonary Gangrene Clinical Course and Pathology*  
By B S Kline, M D, and S S Berger,  
M D (Archives of Surgery, January, 1929,  
p 481)

The lesion in many cases of so-called typical abscess of the lung has been found to be gangrene. Instead of a grayish area of suppuration without appreciable odor, the lesion is ragged, brownish or greenish and penetratingly foul-smelling. The sputum in these cases is foul smelling, grayish brown or grayish green and contains characteristic oral spirochetes, fusiform bacilli and vibrios. In case of true abscess, on the other hand, it is whitish yellow, mucopurulent or purulent, without appreciable odor and contains pyogenic organisms, usually staphylococci. As patients with pulmonary gangrene do not respond well to the treatment for abscess but are frequently cured by arsphenamine therapy the differentiation between these two diseases is imperative. A study of the cases of pulmonary abscess and gangrene observed at Mount Sinai Hospital in Cleveland in the past five years showed 8 cases of multiple embolic pulmonary abscesses, manifestations of a staphylococcus septicemia or pyemia, 9 cases of abscess of the lung caused by pyogenic organisms, not associated with septicemia or pyemia, and apparently aspiratory in type, one third of which followed operation, almost all of which were in infants or children, on the other hand, pulmonary gangrene occurred almost entirely in adults and 3 times as frequently as aspiratory abscess. About one-half of the cases of gangrene occurred after operation. In both aspiratory abscess and gangrene the lower lobes were more frequently involved than the others. Six of nine patients with aspiratory abscess died, whereas eleven of fifteen with gangrene of the lung

recovered. The striking results in gangrene, a much more severe process than abscess, were due to the early recognition of the disease as gangrene and to the prompt and intensive treatment with arsphenamine and arsphenamine preparations. The authors conclude that pulmonary abscess and pulmonary gangrene are separate entities. In spite of distinguishing characteristics these are, however, almost universally considered and treated as one disease. At the Mount Sinai Hospital in Cleveland in the past five years, pulmonary gangrene has been observed three times as frequently as pulmonary abscess. Pulmonary gangrene, although comparatively a much more severe process than aspiratory abscess, if proper treatment is used, offers an even better prognosis than does abscess. There is conclusive evidence that pulmonary gangrene is caused by a group of organisms, notably spirochetes, fusiform bacilli and vibrios, aspirated from the oral cavity. In cases observed clinically, careful examination of the sputum is sufficient to make possible a differential diagnosis between pulmonary abscess and pulmonary gangrene. In cases of pulmonary abscess the sputum is whitish yellow, mucopurulent or purulent, without appreciable odor, and when washed shows pyogenic organisms, usually staphylococci. In cases of pulmonary gangrene, on the other hand, the sputum is foul smelling, grayish brown or grayish green and when carefully washed and properly stained shows the characteristic spirochetes, fusiform bacilli and vibrios. As the patients with pulmonary gangrene do not respond well to the treatment for abscess but are frequently cured by arsphenamine therapy, the differentiation between these two diseases is imperative. Spirochetal pulmonary gangrene may be prevented by proper oral hygiene or therapeutic measures.

*The Treatment of Arthritis* By Francis Cooley Hall (New England Jour. of Med, 1929, p 360).

Hall reports a study of 89 cases of arthritis seen in the Out-Door Department of the Peter Bent Brigham Hospital. Of these cases 80, or 91 per cent, had had the disease more than one year when first seen; 53, or 59 per cent, had had the disease more than two years. There were 36 cases who had been sufferers from 5 to 15 years. The average duration of the disease was about 5 years. Some of these patients had had the arthritis continually active, others had had smouldering activity of the disease with occasional attacks of acute arthritis. All but 7 cases seemed to the writer to be metabolic in origin, and all but 15 cases in the group were diagnosed as atrophic arthritis. In only 7 cases did the arthritis appear to be at all associated with the presence of infection in the body or to be of the infectious type. Of the 89 cases reported 76 per cent have been followed more than one year, 47 per cent have been followed two years or more, only 7 per cent have been followed less than six months. Treatment consisted of doing everything possible to improve the general health of the patient and correcting any abnormality. The correctable factors most commonly present were (1) fatigue, (2) dietary deficiency, (3) endocrine deficiency, (4) constipation, (5) bad body mechanics. Deficient diet was especially common. This method of attack has led to a good result in 66 per cent of cases. "Good" means arrest of the disease or such marked improvement that arrest appears imminent. There were 29 per cent who did fairly well—a total helped of 95 per cent. The author feels that whatever else is done in the way of treatment, these general measures are so important as to be a prerequisite to a high degree of success in treating arthritis. It seems probable that not all arthritis is infectious in origin, but that other factors such as bad body mechanics, deficient diet, deficient elimination, fatigue, endocrine deficiency, may have some etiological or precipitating importance.

*The Circulatory Changes Following Full*

*Therapeutic Doses of Digitalis* By W. Dock and M. L. Tainter, (Proc of Soc. for Exper. Biol. and Med, March, 1929, p 521).

It has been thoroughly established that digitalis diminishes the cardiac output of normal animals. Recent observers have attributed this to a direct cardiac action of digitalis, but earlier workers showed that the action on the peripheral vessels was of greater importance. The relationship of the vascular changes to cardiac output in intact animals has not been clearly established or appreciated. Dock and Tainter have measured the cardiac output of dogs by the Fick and cardiometric methods, and have also observed the changes in arterial pressures, and peripheral organ volumes. Full therapeutic doses of digitalis produce the following changes in the circulation of morphinized dogs. There is an immediate rise in arterial and venous pressure together with a vagal slowing of the heart and a peripheral vasoconstriction. Within 5 minutes the venous pressure begins to fall, although arterial pressure may rise gradually for over half an hour. Severe operative procedures diminish the pressor responses. The diminution in cardiac output continues with the progressive fall in venous pressure for 2 hours or more. The vessels of the skin and intestine remain constricted, but the spleen and liver increase in volume. The latter change indicates a pooling of blood in this reservoir probably as the result of hepatic vein constriction which thus results in diminished venous return to the heart. It is, therefore, concluded that the diminution of cardiac output following digitalization of dogs is due to diminished filling of the heart, as the result of diminished venous return, which in turn is due to the widespread peripheral vasoconstriction and redistribution of blood. There is no evidence that the reduced blood flow is due to a cardiac action of the drug.

*Yellow Fever in West Africa* De Lamar Lectures, 1927-28 By Oskar Klotz (Changes in the Liver)

The clinical characteristics of West African yellow fever, as well as the gross and

microscopical findings coincide with those of the disease in the Americas. From the pathological study we arrive at the conclusion that yellow fever is an infectious disease whose outstanding lesions consist of fatty degenerations, necrobiosis and necrosis affecting in particular the liver, kidney, heart and spleen. Other organs and tissues also suffer, but this influence upon the organism as a whole is much less than that induced in the organs named. Yellow fever per se does not produce inflammatory processes, and in the cases which recover there is no scarring of the affected organs. Cirrhosis of the liver does not follow yellow fever, nor is a contracted kidney a sequel. The injury done is upon the parenchymatous tissues, stroma and vascular tissues do not respond, and in the stage of repair the restitution is accomplished by a regeneration to replace the injured cells. The injury to the liver is usually the most characteristic and serious lesion of the infecting agent. This organ suffers an intense destruction of the liver cells, beginning in the mid-zonal region, as described by Rocha-Lima, and then extending into both the central and peripheral zones. This destructive process may progress to such a degree that very few liver cells remain. The few living liver cells are to be found close to the portal sheath on the outer edges of the lobule, and as a rim of scattered cells about the central vein. Otherwise the entire hepatic structure is in a stage of necrobiosis and necrosis. The liver in yellow fever although suffering extensive necrobiosis and necrosis remains normal in size or even slightly enlarged. This is recognized in the gross specimen and on microscopic examination. The lobules are not collapsed or shrunken, and the individual cells though necrotic are often distended and enlarged. The necrotic liver cells do not appear readily to undergo autolysis. This resistance to disintegration may be in relation to the peculiar degenerative change which the liver cells suffer. In 1890 Councilman described the liver necrosis arising in yellow fever and pointed out that it was characterized by the development of peculiar acidophilic hyaline globules within the cytoplasm of the cells. All who have

studied the pathology of yellow fever have commented upon this product, and have noted that this hyaline material persists during all stages of the disease, as available in human cases. These hyaline spherules vary in size and stain intensely with eosin and other acidophilic stains. They have been mistaken for red blood corpuscles by the casual observer. In this extensive liver necrosis the blood sinuses within the liver lobule are distorted but not obstructed. Thromboses and inflammation are absent and the structures in the portal sheath are undisturbed. On the other hand a disturbance of the reticulo-endothelial system in the liver (Kupffer cells) is to be seen. This varies from a hyperplasia of these cells and a granular degeneration to an exfoliation and marked fatty degeneration with pigment accumulation. The influence of the virus and its toxins upon these cells accounts for the varying grade of jaundice which accompanies yellow fever. Jaundice is a variable sign, and may be misleading if one relies too strongly upon it in establishing a diagnosis. Although the liver suffers so severely in this disease, and the toxins, if such they prove to be, appear to have a selective action on the liver cells, it has not been possible up to the present time to demonstrate the presence of an organism in these tissues. Fatty degeneration is always present, occurring more intensely in the cells in necrobiosis. In the cases which recover the regeneration of the liver parenchyma proceeds with great rapidity, and at the end of convalescence all of the functions of the liver are restored to it. During the height of the attack, bile pigment are unable to pass through the liver lobule and little or none passes into the bowel, bile salts are wanting and a state of hypoglycemia results. The condition in the patient simulates an almost complete hepatectomy. In one or two features the liver of the African negro differs from that of the white European or American. It is noted that the liver in the adult African very commonly shows a grade of cirrhosis of the biliary type. This fibrosis may be present as localized masses about the channels in the portal sheath and may also show some extension into the neighboring lobule. Some



time it is slight and visible only microscopically; but frequently too it is demonstrable on the cut surface of the fresh liver. Besides this, the presence of a considerable collection of lymphocytes and some plasma cells is an almost universal finding in these natives. This condition occurs in individuals dying of causes other than yellow fever. A careful study of various portions of the liver shows that all lobules do not show

the yellow fever changes equally. This irregularity in the intensity of the tissue attack and the distribution within the liver is best seen in these cases in which the lesions are not far advanced. In a number of cases the left lobe is less involved than the right, and may even escape serious injury while the yellow fever lesions are well marked in the lobules of the right lobe.

## Reviews

*The Adrenals: Their Physiology, Pathology and Diseases* By May A Goldzieher, M D, Formerly Professor of Pathology, University of Budapest, Director of Laboratories, United Israel Zion Hospital, Brooklyn, New York 436 pages, 72 figures The MacMillan Company, New York, 1929 Price in cloth, \$7 50

The purpose of this book is to give a full monographic description of the adrenal glands including their normal and pathological morphology and function, the interpretation of morphological changes and functional disturbances and their relation to clinical medicine In clinical medicine today very little attention is paid to adrenal disturbances Practically speaking the only item of adrenal pathology which is taken into consideration by the average physician is that of complete adrenal insufficiency, leading to Addison's disease Outside of this syndrome the idea of adrenal disturbances usually does not occur to the practising physician or surgeon This volume is an attempt to demonstrate from the innumerable contributions of many workers and from the data added by the author, that quite definite conclusions can be drawn in order to establish several other syndromes, besides Addison's disease, which are by no means as rare and unimportant as generally considered Furthermore, in various syndromes which are brought about by the impairment of other organs than the adrenals, the latter also play a secondary rôle, which deserves attention both from a diagnostic and therapeutic point of view Chapter I is devoted to the development of the adrenals, Chapter II to their anatomy and histology, Chapter III to their physiology, Chapter IV to their pathological anatomy, Chapter V to the pathophysiology of the adrenal, and Chapter VI to organotherapy An extensive bibliography follows constituting nearly one-quarter

of the book, but even in this size lacks many references The material offered in this book is full and comprehensive, and fairly up to date The endocrinal relationships of the adrenals are in particular quite fully given The book is illustrated by reproductions of photomicrographs, the majority of which are very poor A few do not correspond to their legends Surely it is better to leave a book unillustrated than to use such poor illustrations as many of these in this book Taken as a whole this monograph is of value in that it assembles much of the newer knowledge concerning the adrenals and their functions into a convenient form for consideration and examination In accomplishing this the author has succeeded in showing that Addison's disease is not the only functional disturbance of the adrenals of clinical importance

*Youthful Old Age How to Keep Young* By Walter M Gallichan With an Introduction by Thurman B Rice, A M, M D, 236 pages The MacMillan Company, New York Price in cloth, \$2 50

This is an extremely superficial book upon old age, relating chiefly to the hygienic management of this part of life The title itself shows the lack of a proper scientific understanding of age, for there could be no greater misnomer than "youthful" as applied to age For age is not a disease but a normal, natural process of involution dependent upon intrinsic causes and factors destined to remove the individual from this world as soon as he has performed his function and is no longer useful to the race Therefore age cannot be youthful, it may be deferred but to apply the term youthful to this period of life is absurd A youthful old age would be truly pathologic Age is solely the antithesis of youth, it is the period of decay and loss of tissue of a life which will soon

tions, particularly in those of nutrition and of reproduction, it is the period of chronic fatigue and, therefore, a period in which one must fight against disillusionment, discouragement or even despair. That this last stage of life may be borne with resignation, even with a certain degree of cheerfulness is a thing to which we all may assent, but to apply the term "youthful" to the period of senescence is about as foolish an appellation as it is possible to use. The discussion in Chapter XII on the renewing of youth through the operations of Voronoff and Steinach is extremely unscientific and unsound. It is evident that the author believes in "rejuvenation" although he has no idea of what it actually means. Such writing upon this subject, in the half-baked way of this author, is misleading and even dangerous. There can be no rejuvenation in the sense of making an individual young again, as Gallichan assumes, it is evident that all that is accomplished by these operations is but a temporary re-erotization, and such may be actually dangerous instead of beneficial. It is evident throughout this book that the author has no scientific knowledge or conception of the thing he is writing about, old age. He is ignorant of its true physiology and pathology. The book is another one of the semi-popular, hot-air, pseudo-hygienic propagandist writings on old age and its prevention that are dangerous in their unscientific presentation of half-truths. The author further shows the alcoholic prejudices of his countrymen by his remarks upon total abstinence, and the therapeutic action of whiskey on old people. In his statement of Page 7 that "the principal causes of an infirm old age are auto-intoxication" the author reveals the colossal ignorance of the true meaning of age that makes this book dangerous.

*Surgical Radiology* By A. P. Bertwhistle, M.B., Ch.B., F.R.C.S. (Edin.), Late Resident Surgical Officer, General Infirmary at Leeds. With an Introduction by D. P. D. Wilkie, O.B.E., F.R.C.S., Professor of Surgery, University of Edinburgh. 142 pages, 21 illustrations. P. Blakiston's Son

& Co., Philadelphia, 1929. Price in cloth, \$3.50.

This work is written to meet the demand for a book on the interpretation of radiograms. Most books are written from the technical standpoint, but in this volume the subject is dealt with from the clinical point of view. An attempt is made to give brief descriptions of the early signs of disease, and it is hoped that their brevity will not make them appear too dogmatic. The author emphasizes the fact that radiology must ever be the handmaiden of the clinician; an x-ray diagnosis is rarely possible, save with some bone conditions. X-rays are often able to confirm those early, unobtrusive signs which are of such paramount importance if an operation is to hold out its fullest prospect of success. There are ten chapters dealing with the skeleton, alimentary system, urinary system, nervous system, respiratory system, nasal system, dental system, vascular system, thyroid and female generative system. The material consists of short concise statements giving the main facts of what the x-rays will show in various conditions. Only a very small part of these are illustrated by radiograms, so that the descriptions are verbal rather than pictorial. It is a convenient little manual of radiological diagnosis and interpretation.

*A Textbook of Oral Pathology* For Students and Practitioners of Dentistry. By Russell W. Bunting, D.D.S., D.D.Sc., Professor of Dental Histology and Pathology, University of Michigan, Ann Arbor. 495 pages, 326 engravings, and 1 colored plate. Lea and Febiger, Philadelphia, 1929. Price in cloth, \$7.00.

The purpose of this book is to present, in as clear and concise a manner as is possible, the nature and significance of the various diseases of the oral cavity which are not fully treated in works on general pathology. In its preparation the author has had in mind, particularly, the students and the practitioners of dentistry, who, having had some preliminary training in the field of general pathology, desire to acquaint themselves with the present knowledge concerning those diseases which are related to their

own special field of activity. A conscientious effort has been made not to lead the reader too far afield in speculation and theorization, but rather to state only those principles which are fairly well established, and as far as possible, to correlate the material presented in such a manner that it may be easily grasped. The plan of the book is, as follows: following an introduction, Chapter II considers the abnormal development and arrangement of the oral tissues, Chapter III treats of abnormalities of dentition, Chapter IV considers malocclusion of the teeth and dento-facial deformities and is written by B. E. Liescher, Chapter V treats of abnormalities in the teeth, Chapter VI of microscopic malformations of the teeth, Chapter VII of organic and inorganic accretions of the teeth, Chapter VIII of abrasion and erosion of the teeth, Chapter IX is taken up with the subject of dental caries, Chapter X with the pathology of dental caries, Chapter XI with diseases of the dental pulp, Chapter XII with diseases of the periodontal membrane, Chapter XIII treats of periodontal diseases beginning in the gingival tissues, Chapter XIV of pyorrhea alveolaris and pericemental abscess, Chapter XV of stomatitis, Chapter XVI of oral diseases as foci of general infection and Chapter XVII of tumors of the oral cavity. The book is well written in a clear and concise style, the material is well chosen, and the abundant illustrations are well selected and for the most part very good.

*Diseases of the Liver, Gall-bladder and Bile-ducts.* By Sir Humphrey Rolleston, Bart, KCB, MD, Hon D Sc, DCL, LL D, Regius Professor of Physics in the University of Cambridge, Emeritus Physician, St George's Hospital, Sometime President of the Royal College of Physicians of London, and John William McNee, DSO, MD, D Sc, FRCP, Associate Physician to University College Hospital. Third Edition, 889 pages, 87 illustrations. MacMillan and Company, Ltd, London, 1929. Price in cloth, \$16 00.

The first edition of the book appeared in 1905, and the second in 1912. In the last fifteen years the advances of knowledge in

the subject, especially in connection with jaundice, the functional tests for hepatic disorder and cholecystography have been so considerable that many changes and additions have been necessary, and these have not been confined to the text, but apply also to the illustrations, of which 54 are new ones. It has also seemed advisable to add summaries of the anatomy and physiology of the liver and biliary tract, to assist in the explanation of changing conceptions of hepatic and biliary disease. Alterations in classification and nomenclature are inevitable, but in such a transitional period these must be gradual to prevent confusion. As is usually the case it would have resulted in a work of greater unity, had this book been entirely rewritten instead of patching old material with new. The joints and patchwork show all too plainly. The first edition of this book was a very valuable contribution, based as it was upon a carefully worked-up literature. The same cannot be said for the present edition. The literature on hepatic disease of the last fifteen years has not been as carefully reviewed, and there are numerous omissions of important work. With the exception of the modern discussion on jaundice, to which especial attention has been paid, much of importance has been overlooked in the recent literature, particularly with reference to the general pathology of the organ. The illustrations are of uneven value. The book is well proof-read and printed. As a survey of the older literature on hepatic disease it still is of value.

*Quain's Anatomy, Volume IV, Part III The Heart.* By Thomas Walmsley, MD, Professor of Anatomy, Queen's University of Belfast. Eleventh Edition. 152 pages and 4 coloured figures, 80 figures. Longmans, Green and Co, London, New York, Toronto. Price in cloth, \$6 00.

The present volume is a memoir on the human heart. It was originally intended that Part III of Volume IV of the present edition should embrace the whole subject of angiology. On mature consideration, however, it was decided that there was not sufficient new material concerning the ar-

teries and veins as to warrant this. Matters were different as far as the heart is concerned, as much new work has been done on the anatomy of the heart, and in certain of its aspects the subject is of importance to the physician as well as to the anatomist. It was decided, therefore, that the chapter on the heart, which was undertaken by Professor Walmsley, should be issued in somewhat altered form as an independent monograph, and that the remaining sections be dropped. The section on the lymphatics, which was written by Professor Blair, will appear elsewhere. This volume therefore brings the present edition to a close, and it is the hope of the editor that it will prove of value to the clinician as well as to the anatomist, both for the information made available for reference, and for the accounts furnished by the author of the genetic system, the vascular arrangements, and other important topics. A full bibliography is given, which it is hoped will be useful to workers on the subject. This is an excellent treatment of the anatomy of the human heart. The material is full and up-to-date, and the illustrations are excellent. It will be very useful to the physician as well as to the student of anatomy.

*Clinical Electrocardiograms Their Interpretation and Significance Mayo Clinic Monograph* By Frederick A. Willius, B.S., M.D., M.S. in Medicine, Section on Cardiology, The Mayo Clinic, Rochester, Minnesota and Associate Professor of

Medicine, The Mayo Foundation, University of Minnesota. 210 pages, 368 illustrations. W. B. Saunders Company, Philadelphia and London, 1929. Price in cloth, \$8.00.

In the preparation of this book the author has attempted to present clinical electrocardiography in a graphic manner, and he hopes that the illustrative examples may aid those whose experience in this field is limited. The attempt has been made not only to present typical records of cardiac disorders, but also to present records which exhibit transitional changes. The text of the book is devoted entirely to the reading of the records and their clinical significance. There is no discussion of the technique of electrocardiography, the preparation of records, theory or the many controversial questions. The illustrations have been chosen carefully from a large material, and are accompanied by detailed legends. Since the object of the book is not only to present records and the principal facts regarding their interpretation, but also to aid the reader in pursuing phases in which he is especially interested, a full bibliography has been added. This book will be of especial interest to the cardiologist for comparative study of records, and also of great value to the medical student who is just taking up the study of electrocardiograms. The many records given here will aid him in interpretation and in acquiring a familiarity with electrocardiographic phenomena.

# College News Notes

## CONSTITUTION AND BY-LAWS OF THE AMERICAN COLLEGE OF PHYSICIANS CONSTITUTION

### ARTICLE I

#### NAME

The name of the corporation shall be the American College of Physicians

### ARTICLE II

The American College of Physicians is incorporated under the laws of the State of Delaware. The location of the corporate office is DuPont Building, 7 West Tenth Street, in the City of Wilmington, County of New Castle, Delaware. The name of the agent therein and in charge thereof is the Corporation Trust Company of America

### ARTICLE III

#### OBJECTS

SECTION 1 The object of the American College of Physicians shall be to establish an organization composed of qualified internists of high standing who shall meet from time to time for the purpose of considering and discussing medical and scientific topics, and who through their organization shall attempt to accomplish the further purposes of (a) maintaining and advancing the highest possible standards in medical education, medical practice and clinical research, (b) perpetuating the history and best traditions of medicine and medical ethics, and (c) maintaining both the dignity and the efficiency of Internal Medicine in its relationship to public welfare

#### POWERS

SECTION 2 Acting through its Board of Regents and Officers subject to the powers and restrictions of its certificate of incorporation, and its By-Laws, the College is empowered to do all and only such acts as

are necessary or convenient to the attainment of the objects and purposes herein set forth, and to the same extent and as fully as any natural person might or could do, to purchase, lease, hold, sell, mortgage, or otherwise acquire or dispose of real or personal property, to enter into, make, perform or carry out contracts of every kind with any firm, person, corporation or association, to do any acts necessary or expedient for carrying on any or all of the objects and purposes of the corporation not forbidden by the certificate of incorporation, or its By-Laws, or by the laws of the State of Delaware, to have offices and promote and carry on its objects and purposes within or without the State of Delaware in other States, the District of Columbia, the territories or colonies of the United States. The corporation shall not have any capital stock, nor shall it be conducted for the purpose of financial profit

SECTION 3 The corporation shall consist of Masters and Fellows. The College may also elect Associates who, however, shall not be members of the corporation nor have a right to vote

The College shall vest its general management in a Board of Governors and in a Board of Regents

### ARTICLE IV

#### MEMBERSHIP

Members of the American College of Physicians shall be of two classes (a) Fellows and (b) Masters

(a) Fellows Fellows shall be members of the medical profession engaged as practitioners, teachers or research workers in Internal Medicine or in any allied specialty who shall have been elected in accordance with the By-Laws and such other rules as the Board of Regents may from time to time adopt—the By-Laws and such other rules may be amended by a vote of two-thirds of the members of the Board of Regents

tion only of internists of such high qualifications, personal and professional, as would entitle them to be rated as fully qualified Fellows

Fellows shall be authorized to use the letters F A C P after their names on professional cards in professional directories and in professional publications

Fellows shall have the right to vote and to hold office

(b) Masters Masters of the American College of Physicians shall be those who have attained the rank of Fellows, and who on account of personal character, positions of influence and honor, eminence in practice or in medical research, or other attainments in science or in the art of medicine are recommended by the Committee on Credentials to the Board of Regents for special and well-earned distinction Such Masters shall be designated as Masters of the American College of Physicians, and shall be authorized to use the letters M A C P. in connection with scientific publications, at professional and academic functions and in connection with their professional activities

Masters shall have the right to vote and to hold office

## ARTICLE V

### ASSOCIATE MEMBERSHIP

SECTION 1 Associates shall be members of the medical profession engaged as practitioners, teachers or research workers in Internal Medicine, or in an allied specialty, who shall have been elected in accordance with the By-Laws and such additional rules as the Board of Regents may from time to time adopt—the By-Laws and additional rules being intended to insure the election to Associateship only of persons whose qualifications are such as to give promise of such subsequent development within the time specified in the By-Laws as would entitle them to election to Fellowship It is intended that Associateship shall be in effect a probationary status from which the holder may be elevated to Fellowship, within a specified period of time, upon presenting the evidence of possessing the qualifications required for election to Fellowship

SECTION 2 Associates shall receive all publications of the College, and may par-

ticipate in the annual Clinical Session of the College, but they shall not be permitted to vote or to hold office

## ARTICLE VI

### AMENDMENTS

Proposed amendments to this Constitution shall first be submitted to the Board of Regents for its recommendation The recommendation of the Board of Regents shall then be presented to the members of the College for their consideration at least thirty days before the annual meeting either through the official publications of the College or by letter

A two-thirds vote of the members voting at an annual meeting shall be necessary to adopt an amendment

## BY-LAWS

### ARTICLE I

#### OFFICERS

SECTION 1 The Officers of the American College of Physicians shall be a President, a President-Elect, a First Vice-President, a Second Vice President, A Third Vice President, a Secretary-General, an Executive Secretary and a Treasurer

SECTION 2 The President-Elect, the First Vice President, the Second Vice President and the Third Vice President shall be elected at the annual meeting of the College, each for a term of one year or until his successor is elected The President-Elect shall enter upon his duties as President at the annual meeting following his election The Secretary-General and the Treasurer shall be appointed by the Board of Regents for a term of one year or until their successors are chosen The Executive Secretary shall be appointed by the Board of Regents

SECTION 3 The President of the College shall preside at all regular and special meetings of the College and Board of Regents, and at all convocations for the conferring of certificates of "Master" and "Fellow" He shall be an ex-officio member of all standing committees He shall appoint within one month after induction to office a Nominating Committee of five, composed of two members of the Board of Regents, two members of the Board of Governors and

one Fellow at large, whose duty it shall be to nominate candidates for the elective offices, Board of Regents and Board of Governors. The selection of nominees for the Board of Governors shall be made after due consideration of suggestions of members from the respective states, provinces or districts which will be represented by the nominees, if elected. The list of nominees for President-Elect and for the first, second and third Vice Presidents shall be submitted to all the Masters and Fellows of the College at least one month before the annual meeting, and the election of all nominees shall be by the members of the College at its annual business meeting. This does not preclude nominations made from the floor at the annual meeting itself.

**SECTION 4** The President-Elect shall keep in close touch with the affairs of the College. He shall be a member of the Board of Regents, and meet with important committees.

**SECTION 5** The First Vice President shall assume the duties of the President in the event of the death, resignation or absence of the President.

**SECTION 6** The Second Vice President shall assume the duties of the First Vice President in the event of the death, resignation or absence of the First Vice President.

**SECTION 7** The Third Vice President shall assume the duties of the Second Vice President in the event of the death, resignation or absence of the Second Vice President.

**SECTION 8** The Secretary-General shall be the adviser to the Executive Secretary. He shall sign certificates and all official documents.

**SECTION 9** The Executive Secretary shall be the business manager of the College. Under the direction of the Board of Regents he shall have supervision of activities and business affairs of the College. He shall (1) act as Secretary to the Board of Regents, the Executive Committee and the Board of Governors, (2) direct the executive offices of the College, maintaining all records such as those of membership, inventories and accounting, (3) collect initiation fees and dues, (4) prepare a budget

covering all expenditures for the organization, said budget to be approved by the Board of Regents or Executive Committee, (5) issue all vouchers for payment of bills on budget authorization, (6) assist in the auditing of the Treasurer's accounts, (7) mail notices, announcements, et cetera, of all regular or special meetings of the College to all members of record, (8) under the direction of the Board of Regents, provide for and have charge of (a) convocations, and (b) annual Clinical Sessions, (9) perform such other duties as are assigned to him by the various governing bodies of the organization.

He shall be bonded in the sum of Five Thousand Dollars, or in such sum as may be designated by the Executive Committee, premium for same to be paid by the College.

**SECTION 10** The Treasurer shall receive all funds of the College and disburse the same on checks, signed by him, upon voucher signed by the Executive Secretary. He shall make a report in writing to the Board of Regents of the moneys received and expended, furnishing a detailed statement of the financial condition of the College at each annual meeting. The Treasurer shall furnish a bond to the Board of Regents in the sum of Ten Thousand Dollars, or in such sum as may be designated by the Board of Regents, for the faithful performance of his trust, premium upon same to be paid by the College.

## ARTICLE II

### BOARD OF REGENTS

**SECTION 1** The Board of Regents shall consist of twenty-three members as follows: The President, the President-Elect, the Vice Presidents, Secretary-General, Treasurer, Chairman of Board of Governors and fifteen members elected from among the Masters and Fellows.

**SECTION 2** The Executive Secretary of the corporation shall be the Secretary of the Board of Regents.

**SECTION 3** The members of the Board of Regents shall each serve for a term of three years and no more than two consecutive terms. The duties of the Board of Regents shall be to:



gents shall be those ordinarily performed by a board of directors of a corporation, namely to transact all detail business required to carry out the objects of the organization, to regulate and to conserve the property interests of the College; to fix initiation fees and annual dues of members; to adopt, from time to time, rules and regulations for the election of Fellows and Associates supplementary to the regulations contained in the By-Laws; to create, appoint and direct all standing committees; to elect editors and committees on publication for all publications of the organization, to call all meetings of the corporation not already provided for; to make arrangements through the Executive Secretary for convocations, the annual Clinical Session, and other meetings, to elect Masters, Fellows and Associates, and to transact all business not otherwise provided for that may pertain to the organization

**SECTION 4** The Board of Regents shall appoint a Committee on Credentials for Fellowship whose duty it shall be to pass upon the qualifications of those proposed for Fellowship and recommend those considered eligible to the Board of Regents. This Committee shall meet annually with the Committee on Credentials for Associateship for joint discussion of the proper interpretation of established standards of eligibility

**SECTION 5** Seven members of the Board of Regents shall constitute a quorum for the transaction of business

**SECTION 6** Regular meetings of the Board of Regents shall occur at least once annually at the call of the President. Special meetings may be convened at any time by the President and the Secretary-General, or on a request made in writing, and signed by fifteen members of the Board of Governors, or by twelve members of the Board of Regents

**SECTION 7** No elective officer or member of the Board of Regents shall be a member of the Board of Governors at the same time

**SECTION 8** In the event of death or resignation of any member of the Board of Regents, his successor shall be elected at

the next regular business meeting of the College, but the Board of Regents may appoint a Master or Fellow to serve as Regent until this election shall have taken place

### ARTICLE III

#### EXECUTIVE COMMITTEE

**SECTION 1.** The Board of Regents shall elect annually, by ballot, five of its members who, together with the President, President-Elect, Secretary-General and Treasurer, shall constitute an Executive Committee. Members of the Executive Committee shall be eligible for re-election

**SECTION 2** The Executive Secretary shall be Secretary of the Executive Committee

**SECTION 3** During the intervals between the meetings of the Board of Regents, the Executive Committee shall exercise all the powers of the Board of Regents in the management and direction of the business and the conduct of the affairs of the corporation, except that it shall not have the power to elect Masters, Fellows or Associates, or to regulate initiation fees or annual dues. It shall keep a record of its proceedings and report the same to the Board of Regents at the next succeeding meeting for its approval. It may, at its discretion, appoint such sub-committees as it may deem necessary or desirable for the proper transaction of the business of the corporation. It may adopt rules and regulations for the conduct of its meetings and activities, not inconsistent with the By-Laws of the College and the laws of the State under which the College is incorporated. It may hold its meetings at such place or places as it may from time to time determine. A majority of the Executive Committee shall constitute a quorum for the transaction of business

### ARTICLE IV

#### BOARD OF GOVERNORS

**SECTION 1** At the annual meeting of the American College of Physicians, the Masters and Fellows in open session shall elect certain of their members to serve on the Board of Governors each for a term of three years, as follows. One from each State and Territory in the United States and its possessions, one from each province

in Canada, and one or more from Mexico, Cuba and other countries of the American Continent as shall be determined by the Board of Regents, one each from the United States Army, Navy and Public Health Service, and one each from the Canadian Army, Navy and Public Health Service

In order to preserve the continuity of the Board of Governors, upon the adoption of this section, the members shall be divided, by lot, into three classes, each class having approximately the same number. The term of office of those members in Class One shall expire in 1928, of Class Two in 1929, and of Class Three in 1930. The tenure of office of members elected to succeed the present members of the Board of Governors shall be three years.

Upon the recommendation of the Board of Regents and the affirmative action of the College at the annual meeting, the number of Governors may be increased by the election of an additional member, or members, to represent a State or Territory, or other geographical unit, in which on account of extent or population it is desirable to have additional members for the better conduct of the work of the Board of Governors. Such additional representation should be geographically distributed in a manner best to fulfill the purpose indicated. The term of new Governors elected in accordance with this provision shall be regulated so as to retain equal distribution and rotation in each group as previously provided.

Should there be no Master or Fellow in any state, territory, province or public service entitled to representation as herein provided for, then such place on the Board of Governor shall remain vacant until such state, territory, province or public service has qualified. The President shall fill all vacancies in the current membership of the Board of Governors who represent the States of the United States, or the Provinces of Canada, or other territories, due to death, resignation or other cause, until such time as successors shall have been elected in the regular manner.

SECTION 2 The Board of Governors shall meet in executive session annually at

the time and place of the annual meeting of the American College of Physicians for the transaction of such business as may come before it. Such business shall include (1) the passing upon the qualifications of candidates for Associateship who have been recommended by the Committee on Credentials of the Board of Governors and the recommendation of those applicants who have received favorable endorsement to the Board of Regents for election, (2) other routine business which may be brought before it by the corporation or the Board of Regents.

Annual meetings shall be called by the Executive Secretary at the direction of the Chairman of the Board of Governors. Special meetings of the Board of Governors shall be called by the Executive Secretary at the direction of the Chairman of the Board of Governors at any other time, at the request of the Board of Regents or fifteen members of the Board of Governors.

SECTION 3 The Board of Governors shall organize and elect its own Chairman and Vice Chairman, the same to serve for terms of three years. Should the membership of the Chairman or the Vice Chairman in the Board of Governors terminate, the office of Chairman or Vice Chairman shall thereby automatically become vacant.

SECTION 4 The Chairman of the Board of Governors shall be a member of the Board of Regents. With the exception of the chairman of the Board of Governors, no Governor shall be a member of the Board of Regents at the same time.

SECTION 5 The Executive Secretary of the College shall be the Secretary of the Board of Governors.

SECTION 6 The Board of Governors shall appoint a Committee on Credentials for Associateship whose duty it shall be to pass upon the qualifications of applicants for Associateship and recommend those considered eligible to the Board of Governors for endorsement and recommendation to the Board of Regents for election.

This Committee shall meet annually with the Committee on Credentials for Fellowship for joint discussion of the proper interpretation of established criteria of eligibility.

SECTION 7. Fifteen members of the Board of Governors shall constitute a quorum for the transaction of business. Voting by proxy shall not be allowed

## ARTICLE V

### ELECTION OF FELLOWS

SECTION 1 A Fellow of the College shall have met the following qualifications and requirements. (a) He shall be more than 29 years of age,

(2) He shall be the possessor of a diploma conferring the degree of M.D, M B, or M D C M, from a medical school acceptable to the Board of Regents, and received at least five years prior to the time of his election,

(c) He shall be a member in good standing in his local, State and national medical societies, except in the case of those not engaged in practice, such as full-time teachers, research workers, etc ,

(d) If a practitioner, he shall be a licensee to practice medicine in his respective State or Province, or a Medical Officer in the Governmental Service, either of the United States or of the Dominion of Canada, in American or Foreign Service, if not a practitioner, he shall be engaged either in scientific medical research or in teaching in a hospital or institution recognized by the Board of Regents,

(e) He shall in no wise, directly or indirectly, either personally or in connection with a firm or institution, be engaged in the improper exploitation of medical service or the results of medical research

### PROPOSAL

SECTION 2 His name shall be proposed in writing by a Master or Fellow of the College, not an officer or member of the Board of Regents, it shall be seconded by another Master or Fellow, and endorsed by the member of the Board of Governors from the State or Province in which he resides, or by the Surgeon-General of the Public Service of which he is a member, or by an officer of the College, or by a member of the Board of Regents His nomination must be accompanied by a written statement made both by the proposer and seconder, containing all of the necessary

qualifications of the candidate. Further, the name of the candidate shall be sent to each Fellow in the candidate's locality, with a request for comments as to the candidate's fitness. The proposer must, moreover, be prepared to add such further information as may be requested by the Committee on Credentials

### PROFESSIONAL QUALIFICATIONS

SECTION 3 (a) In the case of practitioners without teaching or important hospital positions, or of candidates not engaged in the practice of Clinical Medicine (laboratory workers, including roentgenologists), the presentation of an adequate number of case reports and autopsies shall be strictly enforced, along with all other necessary information as to fitness, unless the candidate's nomination is accompanied by a satisfactory thesis or by publications of sufficient number and character to qualify him for Fellowship

(b) In case of the nomination of candidates who are teachers, detailed information shall be required as to the character of the teaching position held, also previous positions, type of teaching, and publications The mere holding of the title of teacher in any institution shall not be accepted without further consideration

(c) In the case of candidates nominated by reason of the holding of important hospital positions apart from teaching, the duration of hospital service, the number of beds under the candidate's personal care, and other pertinent details concerning the character of the candidate's clinical work and publications must be furnished by the proposer

After 1931, a candidate for Fellowship shall be eligible only if already an Associate, except upon recommendation of the Committee on Credentials, by reason of very special qualifications

Nominations, with all required data pertaining thereto, shall be submitted through the Executive Secretary's office at least thirty days in advance of the meeting at which they are to be considered

The credentials of candidates for Fellowship shall be considered first by the Committee on Credentials for Fellowship, which

Committee shall report to the Board of Regents for election, deferment or rejection

Successful candidates shall be so notified immediately, after their election, and shall be urged to attend the next succeeding Convocation, when Fellowships will be formally conferred. The official Fellowship Certificate, signed by the President and the Secretary-General, shall be issued following the Convocation. Acknowledgment of its receipt shall be made upon an official card, signed and dated by each Fellow, and returned to the Executive Secretary, to be added to the official College roll

## ARTICLE VI

### ELECTION OF ASSOCIATES

SECTION 1 An Associate of the College shall have met the following qualifications and requirements

(a) He shall be more than 26 years of age,

(b) He shall be the possessor of a diploma conferring the degree of M.D., M.B., or M.D.C.M., from a medical school acceptable to the Board of Regents, and received at least three years prior to the time of his election,

(c) He shall be a member in good standing in his local, State and national medical societies, except in the case of those not engaged in practice, such as full-time teachers, research workers, those holding official hospital positions, etc.,

(d) If a practitioner, he shall be a licensee to practice medicine in his respective State or Province, or a Medical Officer in the Governmental Service, either of the United States or of the Dominion of Canada, in American or Foreign Service, if not a practitioner, he shall be engaged in an official institutional position in one of the accepted branches of Internal Medicine or in medical research,

(e) He shall in no wise, directly or indirectly, either personally or in connection with a firm or institution, be engaged in the improper exploitation of medical service or the results of medical research

### PROPOSAL

SECTION 2 His name shall be proposed, seconded and endorsed in the same manner

as candidates for Fellowship, and his proposer must submit evidence that he is engaged in Internal Medicine or an allied specialty, or in equivalent research work, with the intent of pursuing such work as a permanent career. After 1931, he may be required to present himself for personal examination, the character of which shall be determined by the joint Committees on Credentials

The credentials of candidates for Associateship shall be considered first by the Committee on Credentials for Associateship, which Committee shall report to the Board of Governors for confirmation or rejection. The Board of Governors shall transmit names confirmed to the Board of Regents for election, deferment or rejection

Successful candidates shall receive at once from the Board of Regents through the Executive Secretary an appropriate official notification of the fact that they have been elected Associates of the College

### TERM OF ASSOCIATESHIP AND ELIGIBILITY

#### FOR FELLOWSHIP

SECTION 3 Candidates elected after the adoption of this section (April, 1929), shall be elected for a term of five years

An Associate so elected shall be eligible for election to Fellowship at the end of three years after his election to Associateship. At the expiration of three years, he shall be notified in writing by the joint Committees on Credentials of his eligibility for election to Fellowship during the next two years, provided he shall meet within that time the requirements necessary for Fellowship. If not elected to Fellowship within five years, his Associateship will automatically cease

## ARTICLE VII

### FEES

SECTION 1 The annual dues or the Life Membership fee shall entitle each Master, Fellow and Associate to privileges of membership of his respective class, to the benefits of the Clinical Session and to the official publications of the College

Masters, Fellows and Associates of the College shall not be required to pay dues to the College after their election

of 65 years, or after they have submitted satisfactory evidence to the Board of Regents to show that they have retired from the active practice of medicine or from scientific medical research

At the discretion of the Board of Regents, without publicity, initial fees or annual dues may be remitted, in whole or in part, as in case of men engaged in purely scientific research, full-time medical teaching, the public service, or in the event of any Master, Fellow or Associate suffering serious disability or financial reverses. In case of change of status to private practice or similarly remunerative occupation, the Board of Regents may require the payment of the usual annual dues

### ARTICLE VIII

#### ENDOWMENT FUND

It shall be the duty of the Board of Regents to provide a plan for securing an adequate endowment, the principal of which shall be held intact and invested in securities approved by the Board of Regents, while the income shall be available for carrying out the purposes of the organization. Such endowment fund shall consist of (1) all moneys received for Life Membership in the College, (2) such moneys as may be set aside by the Board of Regents from time to time from the funds of the College, and (3) such moneys as may be donated directly to the fund

### ARTICLE IX

**SECTION 1** The Board or Regents, through the Executive Secretary, shall issue from time to time a Directory of the College containing the names and addresses of the Masters, Fellows and Associates of the American College of Physicians arranged by States, Provinces and colonies

**SECTION 2** The Board of Regents shall publish a journal devoted to the advancement of Internal Medicine. Other publications may be authorized from time to time by the Board of Regents when it seems desirable or expedient so to do

**SECTION 3** The Board of Regents shall appoint editors and editorial boards to carry out these provisions

### ARTICLE X

#### BUSINESS MEETING

A business meeting of the College shall be held each year, during the week of the annual Clinical Session, for the election of officers, Regents and Governors, and for the transaction of such other business as may be necessary

### ARTICLE XI

#### ANNUAL CONVOCATION

**SECTION 1** The College shall hold an annual convocation for the purpose of conferring the certificate "Master" and "Fellow" upon candidates who have been recommended by the Board of Regents. A Presidential address will be delivered on this occasion

### ARTICLE XII

#### ANNUAL CLINICAL SESSION

**SECTION 1.** The College shall conduct annually in a recognized medical center a session of clinics, lectures and demonstrations devoted to subjects of particular importance to those interested in Internal Medicine and its branches. The Clinical Session is intended primarily for the benefit of the members of the College, and Associates, but physicians and other scientists who are not members or Associates, may, upon invitation by the Board of Regents, attend as guests

**SECTION 2** The Board of Regents shall be responsible for the conduct of the Clinical Session. It shall provide a Chairman who shall appoint suitable committees to organize and conduct the same under the direction of the Board of Regents

**SECTION 3** The Executive Secretary shall be the executive officer of the Clinical Session, and, acting under the direction of the Board of Regents, shall make all necessary arrangements for the meeting

### ARTICLE XIII

**SECTION 1** Any Master, Fellow or Associate of the College may be disciplined or expelled for conduct which, in the opinion of the Board of Regents, is derogatory to the dignity of the College or inconsistent with its purposes. Expulsion must be voted by a two-thirds vote of the Board of Regents at a meeting at which the Master,

Fellow or Associate against whom charges are made shall be invited to be present. In case such Master, Fellow or Associate does not appear, he may be represented in a manner to be determined by the Board of Regents.

SECTION 2 A Master, Fellow or Associate of the organization who is delinquent in dues automatically loses all privileges that he may possess. After two years' delinquency, and notification by the Board of Regents, he may be dropped from the roll of the College.

#### ARTICLE XIV

These By-Laws may be amended by a majority vote of those present at any annual meeting of the members of the College, provided, however, that notice of such amendment has been submitted in writing to the Board of Regents at least thirty days before the time of such meeting.

#### NEW ELECTIONS TO FELLOWSHIP DURING THE 13TH ANNUAL CLINICAL SESSION, BOSTON, MASS., APRIL 8-12, 1929

Abercrombie, Thomas Franklin Atlanta, Ga  
Alter, Samuel M, Los Angeles, Calif  
Andrews, George Clinton, New York, N Y  
Applewhite, Joseph Davis, Macon Ga  
Bacon, Theodore S, Springfield Mass  
Bailey, Cornelius Oliver, Dallas, Texas  
Baker, Herman M, Evansville, Ind  
Baker, William P, Atlanta, Ga  
Balderrry, Frank C, Tucson Ariz  
Barbash, Samuel Atlantic City, N J  
Barron, Moses Minneapolis, Minn  
Baumann, Frieda, Philadelphia Pa  
Bell, Howard H St Louis, Mo  
Bethel, George E, Galveston Texas  
Birkhaug, Konrad E Rochester N Y  
Blincoe, Homer R, Emory University, Ga  
Bortz, Edward LeRoy, Philadelphia Pa  
Bowdoin, Joe P Atlanta, Ga  
Bramard, C Brewster Hartford Conn  
Briscoe, Cornelius DeW Panama R P  
Brown, Joseph S Lewistown Pa  
Brundage, Albert H Woodhaven N Y  
Bruns, Carl H, Denver, Colo  
Burgess, Alexander M Providence, R I  
Bush, Chesley, Livermore Calif

Cady, Lee De, St Louis, Mo  
Carter, Larue D, Indianapolis Ind  
Casparis, Horton, Nashville, Tenn  
Clarke, R Manning, Los Angeles, Calif  
Conklin, Stanley DeWitt, Sayre, Pa  
Cook, George Lindsay, Tampa Fla  
Cornell, Beaumont S, Fort Wayne Ind  
Crossman, Edgar O, Washington, D C  
Cutter, William D, Los Angeles, Calif  
Dalrymple, Richard R, Erie, Pa  
Dalton, Eugene S, Brooklyn, N Y  
Davis, John Dwight, Rochester, Minn  
Davis, III, Nathan Smith, Chicago, Ill  
Davison, Hal McCluncy, Atlanta Ga  
DeWan, Charles H, Sayre, Pa  
Dewis, John W, Boston, Mass  
Dexter, Thurston H, Brooklyn, N Y  
Drake, Eugene H, Portland, Maine  
Durham, Robert H, Detroit, Mich  
Dwyer, Harold V, Highland Park, Mich  
Echols, George L, Milledgeville, Ga  
Enzer, Norbert, Milwaukee, Wis  
Falconer, Ernest Henry, San Francisco, Calif

Farnsworth Earle E Grand Island, Nebr  
Fiedler, Otho A Sheboygan Wis  
Fitts, John B Atlanta Ga  
Freeman, Elmer Burkitt Baltimore Md  
Frost, Kendal, Los Angeles Calif  
Gaarde, Fred W, Rochester, Minn  
Garvey, John Louis Ann Arbor, Mich  
Gerdine, Linton Athens, Ga  
Getz, Lawrence Ancon, Canal Zone  
Gilbert, Quinter Olen, Oakland Calif  
Goforth, John L, Dallas Texas  
Golden, George Morris Philadelphia Pa  
Gonce, Jr, John Eugene Madison Wis  
Gray, Joseph Dewey Augusta Ga  
Green, Crawford Richmond Troy, N Y  
Gutmann, Benjamin New Brunswick N J  
Hamilton, Ronald L Sayre Pa  
Harden, Robert DuR Washington D C  
Hardisty, Richard H W Montreal Que  
Canada  
Hartman, Clifford Clinton Presbury P  
Haskarl, Robert A Brentham Texas  
Hawes, H John R Preston Mass  
Henderson, Arthur T Montreal Que  
Canada  
Henderson, Harry I Salt Lake City  
Harpe, Frederic Karl Westchester N Y

- Herrick, James B, Chicago, Ill  
 Hill, Roy A, Thomasville, Ga  
 Hinton, Charles C, Macon, Ga  
 Hoff, Alfred, St Paul, Minn  
 Holbrook, W Paul, Tucson, Ariz  
 Hollnshed, Ralph K, Westville, N J  
 Hollingsworth, Edward W., Maywood, Ill  
 Hornor, Albert Aurelius, Boston, Mass  
 Howard, Lee, Savannah, Ga  
 Howson, Carl Robert, Los Angeles, Calif  
 Hoyne, Gjeimund, Eau Claire, Wis  
 Huffman, Lester D, Rochester, Minn  
 Hursthal, Lewis M, Boston, Mass  
 Ikeda, Kano, St Paul, Minn  
 Irons, Ernest Edward, Chicago, Ill  
 Jarrell, William Williamson, Thomasville, Ga  
 Jennings, Frank LaMont, Oak Terrace, Minn  
 Johnson, Francis B, Charleston, S C  
 Johnson, Trimble, Atlanta, Ga  
 Jones, E Henry, Youngstown, Ohio  
 Justin, Arthur W, Weehawken, N J  
 Kamp, Joseph C, Casper, Wyo  
 Kaufman, Isadore, Philadelphia, Pa  
 Kaufmann, Joseph, Montreal, Que, Canada  
 Kelley, Ernest, Omaha, Nebr  
 Kerlin, Douglas L, Shreveport, La  
 Kerr, Robert B, Manchester, N H  
 King, S Edward, New York, N Y  
 Kinlaw, William Bernard, Rocky Mount, N C  
 Kirklin, Byrl Raymond, Rochester, Minn  
 Knox, Robert A, Washington, Pa  
 Krause, Allen K, Baltimore, Md  
 Lamont, George A, Vancouver, B C  
 Lawrence, Charles H, Boston, Mass  
 Lea, Jesse Worthy, Jackson, La  
 Lettenberger, Joseph, Milwaukee, Wis  
 Levine, Samuel A, Boston, Mass  
 Linde, Joseph I, New Haven, Conn  
 Lippincott, Leon S, Vicksburg, Miss  
 Longo, Thomas J, Brooklyn, N Y  
 Lord, Frederick Taylor, Boston, Mass  
 Lummis, Frederick R, Houston, Texas  
 Lyman, Warren S, Ottawa, Ont, Canada  
 MacNevin, Malcolm Graham, New York, N Y  
 Magan, Percy T, Los Angeles, Calif  
 Magath, Thomas Byrd, Rochester, Minn  
 Mann, Fred W, Houlton, Maine  
 Margolies, Michael, Coatesville, Pa  
 Mariette, Ernest Sidney, Oak Terrace, Minn  
 Markson, David Edmund, Chicago, Ill  
 Marvel, Jr, Philip, Atlantic City, N J  
 Maslon, Morris, Glens Falls, N Y  
 McCartney, James Lincoln, New York, N Y  
 Menagh Frank R, Detroit, Mich  
 Mendelson, Ralph Waldo, Albuquerque, N M  
 Menninger, William C, Topeka, Kansas  
 Middleton, William S, Madison, Wis  
 Mills, Charles Wilson, Tucson, Ariz  
 Mitchell, Edward Clay, Memphis, Tenn  
 Moffatt, Charles F, Montreal, Que, Canada  
 Morgan, Hugh J, Nashville, Tenn  
 Morris, Roger S, Cincinnati, Ohio  
 Murphy, Francis D, Milwaukee, Wis  
 Naurison, James Z, Springfield, Mass  
 Nicholson, Jr, Samuel T, Pottstown, Pa  
 Norfleet, William J, Shreveport, La  
 Odom, Cleve C, Corozal, Canal Zone  
 O'Leary, Cornelius A, Long Island, N Y  
 Overstreet, Samuel A, Louisville, Ky  
 Pendleton, Judson P, Brooklyn, N Y  
 Perry, Matthew White, Washington, D C  
 Phillips, Howard T, Wheeling, W Va  
 Pinney, George L, Hastings, Nebr  
 Puestow, Karver L, Madison, Wis  
 Pund, Edgar R, Augusta, Ga  
 Reading, Boyd, Galveston, Texas  
 Reed, Edward U, San Pedro, Calif  
 Reitzel, Raymond J, Galveston, Texas  
 Reuter, Carl H, Springfield, Ohio  
 Riecker, Herman H, Ann Arbor, Mich  
 Riggs, Charles Edward, Washington, D C  
 Robey, William Henry, Boston, Mass  
 Robinson, Lisle B, Atlanta, Ga  
 Roen, Paul B, Los Angeles, Calif  
 Rosamond, Eugene, Memphis, Tenn  
 Rosenberger, Andrew I, Milwaukee, Wis  
 Rowe, Paul H, Minot, N D  
 Sanders, Audley Owenton, Palo Alto, Calif  
 Schnabel, Truman G, Philadelphia, Pa  
 Scott, David Patteson, Lynchburg, Va  
 Severinghaus, Elmer L, Madison, Wis  
 Shambaugh, Noel F, Ann Arbor, Mich  
 Sherman, George Alexander, Pontiac, Mich  
 Sherrill, James W, LaJolla, San Diego, Calif  
 Siegel, Alvin E, Philadelphia, Pa  
 Sloan, LeRoy H, Chicago, Ill  
 Smith, Claiborne T, Rocky Mount, N C

Smith, George C, Mansfield, Ohio  
 Snure, Henry, Los Angeles, Calif  
 Spear, Louis M, Boston, Mass  
 Stealy, Clair Lazarus, San Diego, Calif  
 Steele, George L, Springfield, Mass  
 Stevens, Martin L, Asheville, N C  
 Stoll, Henry F, Hartford, Conn  
 Sweet, Earl, Los Angeles, Calif  
 Tappan, John W, Fort Stanton, N M  
 Thomas, Anne H, Philadelphia, Pa  
 Thomas, Roy E, Los Angeles, Calif  
 Trippe, Clarence Morton, Asbury Park, N J  
 Ulrich, Joseph M, Akron, Ohio  
 Unger, Isedor Mack, Ithaca, N Y  
 VanValzah, Robert, Madison, Wis  
 Ware, Edward, Richmond, Los Angeles  
 Calif  
 Waters, Charles A, Baltimore, Md  
 Watterson, Walter H, LaGrange, Ill  
 Wesman, Samuel Arthur, Minneapolis,  
 Minn  
 Weiss, Hiram B, Cincinnati, Ohio  
 Welch, Francis J, Portland, Maine  
 Willard, Luvia M, Jamaica, N Y  
 Wilmer, Harry L, Philadelphia, Pa  
 Yaguda, Asher, Newark, N J

**NEW ELECTIONS TO ASSOCIATE-  
 SHIP DURING THE 13TH ANNUAL  
 CLINICAL SESSION, BOSTON,  
 MASS. APRIL 8-12 1929**

Allen, Edgar Vannice, Rochester, Minn  
 Anderson, Edward W, Rochester, Minn  
 Armstrong, Eugene L, Los Angeles, Calif  
 Barton, Robert M, Dallas, Texas  
 Bates, Clarence E, Oklahoma City, Okla  
 Bauer, Theodore I, Lansing, Mich  
 Behneman, Harold Mayo F, San Francisco,  
 Calif  
 Benson, Carl S, Binghamton, N Y  
 Berlinghof, Clifton H, Binghamton, N Y  
 Bosworth Robinson, Rockford, Ill  
 Bryans, Herbert L, Pensacola, Fla  
 Callaway, Guy D, Springfield, Mo  
 Cassel, Homer D, Dayton, Ohio  
 Chambers, John S, Lexington, Ky  
 Chase, Harrison A, Brocton, Mass  
 Cook, Ben H, Norman, Okla  
 Cring, George V, Portland, Ind  
 Dechen, Frank, Bloomington, Ill  
 Decker, Karl H, Marshall, Wis

Dyer, Garland L, Buechel, Ky  
 Evans, Theodore S, New Haven, Conn  
 Fancher, James Kenneth, Atlanta, Ga  
 Gable, James J, Norman, Okla  
 Gibson, George G, Wilkesburg, Pa  
 Guardia, Tomas Guardia, Panama, R P  
 LaBarge, Oza Joseph, Salt Lake City, Utah  
 Leverton, Reuben L, Syracuse, N Y  
 Levy, Maurice, Denver, Colo  
 Makepeace, True Edgecomb, Farmington,  
 Maine  
 Nelson, Luther T, Portland, Ore  
 Olch, Benedict, Dayton, Ohio  
 Piper, John Obed, Waterville, Maine  
 Powell, Vernon E, Atlanta, Ga  
 Quirk, John T, Piqua, Ohio  
 Rathe, Herbert W, Waverly, Iowa  
 Rawls, William Bryant, New York, N Y  
 Ruddock, John C, Los Angeles, Calif  
 Sims, Lewis C, Dallas, Texas  
 Sward, Blanton P, Roanoke, Va  
 Silverberg, Sigmund Benjamin, Buffalo,  
 N Y  
 Smith, Cyril M, Duluth, Minn  
 Smith, Munford, Los Angeles, Calif  
 Spangelberger, Mathew A, Denver, Colo  
 Stevenson, Edgar Melvin, Bloomington, Ill  
 Stober, George Washington, Cleveland,  
 Ohio  
 Striker, Cecil, Cincinnati, Ohio  
 Tetdstrom, Milo K, Anaheim, Calif  
 Twiss, John Russell, New York, N Y  
 Wahl, Ernest F, Thomasville, Ga  
 Waldbott, George L, Detroit, Mich  
 Warren, Charles William, Clifton Springs,  
 N Y  
 Weiss, Clifford R, Dayton, Ohio  
 Wetterberg, Louis F, Woodbridge, N J  
 Yntema, Stuart Sigmund, Mich

**Report of Meeting of the  
 BOARD OF REGENTS  
 during the  
 BOSTON CLINICAL SESSION  
 April 8-12, 1929**

The Board of Regents met at the Hotel  
 Huntington in Boston, Mass., on April 8, 1929,  
 for the purpose of discussing the report of the  
 committee on the proposed changes in the  
 curriculum of the medical schools of the  
 United States.



Eric K Bartholomew, Chicago, Ill 12/18/28

Frank W Fleischaker, Louisville, Ky, 11/26/28

Bryce Fontaine, Memphis, Tenn, 3/31/29

Joseph Goldberger, Washington, D C, 1/17/29

Marinus L. Holm, Lansing, Mich, 12/14/28

John L. Macumber, Brooklyn, N Y, 12/22/28

Enoch H Miller, Liberty, Mo, 10/8/28

Charles L Minor, Asheville, N C, 12/26/28

Eugene W Murray, Newark, N J, 9/18/28

J C Taylor, Chelsea, Okla, 3/4/29

Jacob Wolf, Pittsburgh, Pa, 11/19/28

The following resignations of Associates were accepted

Edward S Babcock, Sacramento, Calif

Paul C Carson, Wichita, Kansas

George H Hess, Uniontown, Pa

H L Ulbrich, Detroit, Mich

The life membership of Dr John G Ryan, of Denver, who has subscribed to the Life Membership Fund, was reported

Invitations for the Annual Clinical Session of the College in 1930 were received from Chicago, Richmond, Indianapolis, Denver, Cincinnati, New York and several other cities

A resolution was adopted, providing that the Convocation ceremonies shall be shortened and simplified, and the present plan of repeating the College Pledge eliminated

The Executive Secretary, Mr Loveland, presented the financial report of the College and the Budget for the ensuing year The financial report was presented to all members of the Board of Regents in mimeographed form, and the detail of receipts and expenditures thoroughly explained The entire report had been audited by the public accounting concern, Lybrand, Ross Bros & Montgomery, and consisted of the Cash Statement, Cost Analysis of ANNALS OF INTERNAL MEDICINE, Volume I, Balance Sheet for December 31, 1928, Income and Expense Statement of the General Fund, December 31, 1928, Endowment Fund Statement, Record of Investments, Composite and Detailed Estimates of Income and Expenditures for 1929 A condensed financial report follows

#### *BALANCE SHEET, December 31, 1928*

##### ASSETS

Cash in bank and on hand		\$29,114 49	
Bonds owned		16,626 51	
Accrued interest on bonds		251 87	
Inventory of keys, frames, pledges, etc		975 95	
		<hr/>	
		\$46,968 82	
Deferred expenses for the Thirteenth Annual Clinical Session (Paid in advance of 1929)		142 05	
Furniture and equipment	\$2,895 30		
Less allowance for depreciation	305 54	2,589 76	
	<hr/>	<hr/>	\$49,700 63

##### LIABILITIES

Deposits by candidates, applications pending		\$ 3,830 00	
Deferred income			
Advance collections for exhibits, Thirteenth Annual Clinical Session	\$1,253 70		
Advance subscriptions, Vol III, ANNALS OF INTERNAL MEDICINE	55 25	1,308 95	
	<hr/>	<hr/>	\$ 5,138 95

## FUNDS

Endowment Fund	4 100 00	
General Fund	40,461 68	\$49 700 63

*GENERAL FUND, INCOME AND EXPENSES*

For the year ending December 31, 1928

## Income

Initiation fees	\$12,866 00
Annual dues	20,370 55
Interest on bank deposits	1,314 71
Income from bonds owned	512 62
Income from Endowment Fund	171 00
Profit from miscellaneous sales of keys, frames, pledges, etc , etc	1,156 19

\$36 391 07

## Expenses

Twelfth Annual Clinical Session	
Expenses, including salaries, printing, supplies, entertainment, reporting, traveling expenses, speakers, etc	\$13,206 30
Deduct, Income from Guest Fees, Exhibits, etc	4,126.47

Net expenses	9 070 81
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## Annals of Clinical Medicine

Expenses including balances paid publishers and counsel fees	6 573 02
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Forward	\$15 652 85	\$36 301 07
Forward		\$36 301 07

## Annals of Internal Medicine

Expenses	
Salaries	\$ 3,301 58
Communications	705 12
Office Supplies and Stationery	181 13
Printing	10,803 67
Traveling Expenses	42 50
Miscellaneous	124 88
	\$15 242 88

Deduct	
Subscriptions	12 187 71
Advertising	605 26
	12 792 97

Net Expenses	2 449 78
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## Treasurer's Office

Expenses including clerical service, supplies, etc.	\$75 71
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## Executive Secretary's Office

Expenses	
Salaries	7 25 40

Communications	891 54	
Office supplies and stationery	414 04	
Printing . . . .	724 88	
Rent and maintenance	1,627.81	
Traveling expenses, including Regents	1,235 69	
Miscellaneous	495.44	12,594 40

Year Book and Supplement		
(Cost of production and distribution)	518 15	
Annals of Internal Medicine, distributed to life members	42 00	
Depreciation on equipment etc	286 91	\$32,122 91
Net income for the year		\$ 4 268 16

A resolution was adopted providing that a Finance Committee be appointed by the Chair annually to act for the succeeding year on financial matters. Members of the Finance Committee for 1929-30 are

- Charles G Jennings, Chairman
- Clement R Jones
- William Gerry Morgan
- Leonard Murray
- Maurice C Pincoffs

Dr Aldred Scott Warthin, Editor of ANNALS OF INTERNAL MEDICINE, reported that Volume II of the Journal has been increased three hundred pages over previous volumes, which, naturally, has increased the cost of printing and distribution. The College News Notes Section has been developed with the assistance of the Executive Secretary, who has also increased the circulation from approximately fourteen hundred to twenty-two hundred during the past year and a half. By resolution regularly adopted, the Board of Regents authorized the Editor to continue the ANNALS OF INTERNAL MEDICINE with a maximum of fifteen hundred pages per volume and to maintain the News Notes column at approximately their present volume.

Dr George Morris Piersol, Chairman of the Committee on Credentials, presented the report of his Committee on their action on a total of 262 applications for Fellowship. The list of selections included 193 Fellows, said list being printed elsewhere in this Journal. By a resolution unanimously adopted, the report of the Committee was approved by the Board of Regents.

In recognition of their positions of influence, honor and eminence in practice, or of medical research and distinguished service to the College, the following were elected to Mastership, upon the recommendation of the Committee, or by resolution

- Alfred Stengel, Philadelphia, Pa
- Charles F Martin, Montreal, Que
- Charles G Jennings, Detroit, Mich
- Aldred Scott Warthin, Ann Arbor, Mich
- Frank Smithies, Chicago, Ill

Dr John H Musser presented a report on group clinics and the advisability of the American College of Physicians undertaking the classification of such clinics. It was resolved that a Committee of three of the Board of Regents be continued and requested to make further report at a later meeting.

The Executive Secretary presented a report on the facilities of Minneapolis for handling the 1930 Clinical Session. After discussion by Dr S Marx White, a resolution was adopted, selecting Minneapolis for the Clinical Session for 1930, during the week of February 10. A subsequent resolution was adopted appointing Dr S Marx White the General Chairman of Arrangements.

Dr Clement R Jones, Pittsburgh, Pa, and Dr George Morris Piersol, Philadelphia, Pa, were reappointed by the Board of Regents as Treasurer and Secretary-General respectively for the succeeding year.

The Executive Secretary presented a list of members who have been delinquent for two years or more, pointing out, in accordance with the provisions of the By-Laws,

such members had lost their standing and were subject to being dropped from the College roll. He advised that various notices had been sent each member and every effort had been made to have them maintain their memberships. By resolution regularly adopted, it was resolved that this list of delinquent members be dropped from the roll, but that the Executive Secretary be authorized to reinstate such members as pay their dues up to and before September 1, 1929.

The Executive Secretary announced gifts of publications to the College Library by the following

Philip B. Matz  
William R. Bathurst  
Miles J. Breuer  
Hyman I. Goldstein  
Grafton Tyler Brown  
Ralph O. Clock  
Murray B. Gordon  
Henry J. John  
Aaron Parsonnet  
Lea A. Riely  
Harold Swanberg  
Carl V. Vischer  
Raymond J. Reitzel  
I. S. Trostler  
F. M. Pottenger

It was pointed out that Dr. F. M. Pottenger had contributed a complete list of all of the books of which he is author to the College Library. A resolution embodying a vote of thanks to each contributor was unanimously adopted.

Dr. S. Marx White presented a report of the Committee of the American Hospital Association on Clinical Records. The said report was the result of a conference among representatives from the American Hospital Association, the American College of Physicians, the American College of Surgeons, the American Medical Association and the Association of Record Librarians of North America.

The Chairman of the Committee on Credentials presented a list of fifty-four physicians who were recommended to the Board of Regents for election to Associateship. By resolution regularly adopted the elec-

tions were made. (This list is printed elsewhere in this Journal.)

Dr. Sydney R. Miller, Chairman of the Committee on Constitution and By-Laws, reviewed in detail the amendments being suggested for adoption at the General Business Meeting. These were discussed freely, and a motion adopted to recommend them for approval by the Fellows at large. (The amended Constitution and By-Laws is printed elsewhere in the Journal.)

A resolution was adopted, recommending to the body of the College after the adoption of the amendments to the By-Laws, that two Governors, instead of one, be appointed from the States of California, Illinois, New York and Pennsylvania, because of extent of territory or vastness of population, the precise division of the states to each Governor to be left to the Chairman of the Board of Governors.

The matter of a suitable Mastership Certificate was deferred for a full meeting of the Board of Regents at some future date.

The following Executive Committee was elected by the Board of Regents:

John H. Musser, Chairman  
Sydney R. Miller  
James Alex. Miller  
George Morris Piersol  
John Phillips  
F. M. Pottenger  
Alfred Stengel  
Aldred Scott Warthin

The following Committees were reappointed with their present personnel:

Committee on Credentials for Fellowship  
Committee on Constitution and By-Laws  
Committee on Hospital Libraries

The following Committees were voted to be discontinued due to lack of activity and need or completion of their duties:

Committee on Medical Education and Specialization

Public Relations Committee

Committee on Publication of the Journal

Committee on Student Activities

The same of the following Committees was authorized to continue their work during the next year: Committee on the

its duties extended to assist the Executive Secretary both in censoring advertisements in the Journal and exhibits at the Annual Clinical Session. The present personnel of this Committee was continued.

By resolution, the President was empowered to appoint a Committee on Directory to assist in the determination of the contents for the new 1929-30 Directory. A resolution was adopted providing that the Board of Regents direct the attention of the Committee on Directory to the probable desirability of very much limiting the amount of space taken by published titles of members so as to limit the size of the Directory, reduce its cost and avoid the appearance of display.

The Executive Secretary was requested to adopt some simplified method of notification of members of nominations, said system to be approved later by the Board of Regents.

Report of Meetings of the  
BOARD OF GOVERNORS  
during the  
BOSTON CLINICAL SESSION  
April 8-12, 1929

Meetings of the Board of Governors were held April 8, April 9, and April 10. The members of the Board from a majority of the States and Provinces were present. The Chairman, Dr. Charles G. Jennings, of Detroit, in his remarks to the Board at its opening meeting said in part, "I want to emphasize the enormous amount of constructive work performed on the part of the Officers, the Regents and the Board of Governors, the result of which has been the gratifying development of the College. The most outstanding event of the year has been the extension of the College in a very emphatic way into the conservative Eastern states the meeting in Boston being evidence of the interest and real enthusiasm aroused for the College in this locality. The College cannot but thank Dr. Martin, President of the College, most gratefully for his efforts, because to him entirely, his endeavors, personal visits, correspondence, etc., is due this credit for the interest in membership of those in the academic centers of the East.

The College has extended its influence until it is in reality the 'College of American Physicians', and it now has ample representation from every important district, and the Board of Governors has become a very important body in the conduct and development of the organization. It has the support of the whole United States and Canada. It behooves us to conduct the affairs of the organization so as not to take any action that would diminish the interest of any locality."

The Executive Secretary, Mr. E. R. Loveland, presented his annual report to the Board of Governors, including details concerning the new headquarters in Philadelphia, to which all members are invited to come whenever in Philadelphia, the routine work of the Executive Offices, new equipment installed for the better conduct of the College work, the activity of the Executive Offices in promoting advertising in *ANNALS OF INTERNAL MEDICINE* and in increasing the subscriptions to this publication, and a complete report of the finances of the organization.

Mr. Loveland further called attention to the Endowment Fund, the principal of which is made up of life membership fees contributed by members. This fund, though small (\$4,100.00), is being regularly added to whenever a new member subscribes to Life Membership and pays the prescribed fee. According to the Minutes of the Board of Regents, the following provision is made for life memberships: "In lieu of annual dues, a Master or Fellow may become a life member of the College upon the payment of \$500 in cash or \$100 each year until \$500 has been paid. In case a member desires to pay for life membership by paying \$100.00 yearly for five years, his annual dues cease when he has paid three annual payments of \$100 each. The annual dues and the life membership fee shall entitle each Master and Fellow to privileges of membership of his respective class, to the benefits of the Clinical Session and to receive the official publications of the College."

By resolution unanimously adopted, the Board of Governors confirmed the action of the Chair in appointing the following

Nominating Committee for nominations to the Board of Regents

W Blair Stewart, Chairman, Atlantic City, N J

Allen A Jones, Buffalo, N Y

Samuel E Munson, Springfield, Ill

E L Crispin, Los Angeles, Calif

Clarence M Grigsby, Dallas, Texas

At a later meeting of the Board of Governors, this Committee brought in the following nominations for members of the Board of Regents, which candidates were unanimously elected

For term expiring 1932

Noble W Jones, Portland, Oregon

S Marx White, Minneapolis, Minn

David P Barr, St Louis, Mo

Maurice C Pincoffs, Baltimore, Md

Arthur R Elliott, Chicago, Ill

Amendments to the Constitution and By-Laws were thoroughly discussed and recommendations made to the Board of Regents. At a later conference between the Board of Regents and the Board of Governors, complete agreement was reached as to the exact amendments to be recommended to the General Business Meeting

The Board of Governors received the report of the Committee on Credentials for Associateship, recommending for election a list of fifty-four physicians. The Board of Governors adopted a resolution unanimously recommending this list to the Board of Regents for election, which list was subsequently submitted to the Board of Regents and elected. (*This is published elsewhere in the Journal*) The Executive Secretary, Mr Loveland, presented a list of delinquent members, who according to provisions of the By-Laws and regulations of the College were subject to being dropped because of two or more years of delinquency. The list was reviewed by each Governor, in order that he might intervene in an effort to have especially desirable members on this list pay their delinquent dues and retain their memberships.

The Board of Governors entered into a general discussion concerning the number of guests (non-members) who attend the Annual Clinical Sessions sometimes in each

numbers as to exclude some members of the College from the more popular clinics. It was pointed out that a guest fee of \$5.00 is considered too small, and that only guests who have official invitations from the College should be admitted. A resolution was adopted requesting the Chairman Dr Charles G Jennings, by virtue of his office to take this matter up with the Regents, and express the views voiced by the Board of Governors.

#### Report of the General Business Meeting

of the  
AMERICAN COLLEGE OF PHYSICIANS  
Boston, Mass  
April 11 1929

President Charles F Martin presided. After reading of the Minutes of the previous meeting by the Executive Secretary, Mr Loveland, and approval by the Body, reports of the Committees and Officers were received. Dr Aldred Scott Warthum, Editor of ANNALS OF INTERNAL MEDICINE, reported upon the Journal in considerable detail. He said in part, "The past year has been the most successful year in the history of the Journal. The material submitted has increased and the quality has been increasingly good. The Executive Secretary's office has increased the number of subscriptions fully fifty per cent over what they were in the beginning of Volume I of the new Journal and the present Volume II has been increased three hundred pages in size. The Journal has been distributed

on our former journal, "Annals of Clinical Medicine" and worked out the details for the continuation of the new journal, "Annals of Internal Medicine," reported briefly to the membership the details of the relations of the College with the former publishers, the Williams & Wilkins Company of Baltimore, Maryland, and presented the facts dealing with the financial and legal termination of the publishing contract of that firm. Dr Stengel pointed out that some members had been of the erroneous impression that the College had entered into and lost a legal suit with the former publishers. He pointed out that this was incorrect, that the settlement of the publishing contract was made to the satisfaction of the College and without court proceedings. Associates of Dr Stengel on this Committee were Doctors L. F. Barker, George Morris Piersol, Clement R. Jones and Mr. E. R. Loveland.

The Treasurer, Dr. Clement R. Jones, presented a joint financial report of the College for his office and that of the Executive Secretary. The essential details of this report are printed in connection with the report of the meetings of the Board of Regents.

President Martin, in commenting upon the finances of the College, pointed out the fact that the Fellows of the College, by the payment of initiation fees and annual dues, are making it possible for younger men, and men with small incomes, due to full-time teaching, full-time laboratory work, or service in the Medical Corps of the Army, Navy and Public Health Services, to become Associates or Fellows, that sufficient income is needed to maintain respectable offices to adequately carry on the work, and to have good annual clinical meetings. He stated that during the year, on several occasions, careful analysis had been made of the finances, with a view to reducing the fees and dues, if possible. The findings had indicated that it did not seem advisable to reduce the income of the organization, especially in view of the amended By-Laws, which may have the effect of diminishing the number of new members during the next few years. He paid tribute to the ex-

cellent Exhibit at the Boston Clinical Session, arranged through the efforts of the Executive Secretary, Mr. Loveland, and stated that the income therefrom would be a very material contribution toward the expenses of the Boston Session.

Dr. Sydney R. Miller, Chairman of the Committee on Constitution and By-Laws, at the direction of the meeting, presented the amendments to the Constitution and By-Laws, which, after being read and explained, were by resolution unanimously adopted (the amended Constitution and By-Laws are printed elsewhere in the Journal). The most important changes in the amended Constitution and By-Laws are:

- 1 A proper reassignment of text between the Constitution and By-Laws,

- 2 A clarification of the statements regarding the classes of membership,

A change in the provisions for election of members of the Board of Regents by the Fellows of the College as a whole instead of by the Board of Governors,

- 4 Constitutional provision for the appointment of a Nominating Committee within one month after each annual business meeting for the preparation of list of nominees for the elective offices, the Board of Regents and the Board of Governors,

- 5 The elimination of the application form, and a substitution of a system of proposal, seconding and endorsement of new members,

- 6 A clarification of the requirements for membership,

- 7 Elimination of unnecessary Articles or Sections.

The Nominating Committee presented the following list of nominations for the elective offices for 1929, which list, after no nominations were offered from the floor, was subsequently unanimously elected.

President-Elect—Sydney R. Miller, Baltimore, Md.

1st Vice President—Aldred Scott Warthin, Ann Arbor, Mich.

2d Vice President—F. M. Pottenger, Monrovia, Calif.

3d Vice President—Logan Clendenning, Kansas City, Mo.

Dr John H Musser, who was made President-Elect at the New Orleans Clinical Session in 1928, was at this time inducted as the President of the College for 1929-30. A unanimous rising vote of appreciation was taken on the behalf of the American College of Physicians to the retiring President Dr Martin, for his excellent service and his great interest in the organization.

Dr W Blair Stewart, Chairman of the Nominating Committee for members of the Board of Governors, presented the following nominations, which were unanimously elected.

#### Term Expiring 1932

Edgerton L Crispin, (Southern) California—Los Angeles

Josiah N Hall, Colorado—Denver

Oliver Osborne, Connecticut—New Haven

William Gerry Morgan, Dist of Columbia—Washington

Ernest E Laubagh, Idaho—Boise

Samuel E Munson, (Southern) Illinois—Springfield

Roscoe H Beeson, Indiana—Muncie

Thomas Tallman Holt, Kansas—Wichita

Roger I Lee, Massachusetts—Boston

Adolph Sachs, Nebraska—Omaha

Leander A Riel, Oklahoma—Oklahoma City

\*Edward J G Beardsley, (Eastern) Pennsylvania—Philadelphia

Edwin Bosworth McCready, (Western) Pennsylvania—Pittsburgh

John O Manier, Tennessee—Memphis

G G Richards, Utah—Salt Lake City

Irber Elliott, Ontario—Toronto, Canada

William M James, Panama and the Canal Zone

#### Term Expiring 1931

\*James G Carr (Northern) Illinois—Chicago

Harvey Beck, Maryland—Baltimore

\*Harlow Brooks, (Eastern) New York—New York

#### Term Expiring 1930

\*Hans Lisser, (Northern) California—San Francisco

A Comingo Griffith, Missouri—Kansas City

Edward O Otis, New Hampshire—Exeter

Charles H Cocke, North Carolina—Asheville

Clarence H Beecher, Vermont—Burlington

Ex Officio

M W Ireland, United States Army

Charles Edward Riggs, United States Navy

Hugh Cummings, United States Public Health Service

A voted of thanks on the part of the College was extended to the Boston Committees and various organizations, to the ladies, to the Hotel Statler, and to the press for their contributions to the success of the Boston Session.

#### ANNUAL BANQUET OF THE COLLEGE AT BOSTON

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\*Elected in accordance with provisions of the amended By-Laws and recommendations of the Board of Regents for additional representation in these states on account of extent, or population making it desirable to have additional members for the better conduct of the work of the Board of Governors.



was given for 375, with a leeway of ten per cent increase, if necessary. By Thursday afternoon at three o'clock, about four hundred tickets had been sold, and it was decided that the guarantee made to the Hotel was correct and satisfactory. Provision for 410 were made by the Hotel when setting the banquet Thursday evening. When the doors were opened, nearly 100 physicians, with their guests, appeared **WITHOUT TICKETS**, with the result that the total attendance was raised to 498, with tables set for 412. Tribute should be paid to the prompt arrangements by which tables were brought in by the Hotel Statler and every one seated in a remarkably short time. Fortunately, the Hotel was able to serve, without delay, every one with the regular banquet menu—a very excellent dinner.

Three tables in the center of the banquet hall, and near the speaker's table, were reserved for special guests of the College and a "reserved card" placed on each. When the crowded conditions of the banquet hall were realized, some attendants at the banquet, without consideration of the reserved tables, or in error, took their seats at the reserved tables, before the guests had arrived. Quite naturally, the head waiter had to request them to move to other tables, for our guests, for whom the tables had been reserved, could not be expected to be seated elsewhere, or to remain standing while additional tables were set. A few members, unmindful of the difficulties caused by those who had not purchased their tickets in advance and unthoughtful of the work of the local Committee and the Executive Secretary, lodged vigorous protests and found unwarranted fault with the Committee of Arrangements.

This little editorial is in way of explanation, and an urgent request that individuals, particularly members of the College, shall have charity in sufficient measure to bear with such unavoidable conditions and will in the future procure their tickets in advance as requested. The solution of these difficulties in the future would seem to be corrected if we close the sale of tickets for the banquet twenty-four hours in advance, and admit at the doors only those who have

secured their tickets. The management was in no way responsible for the delay of ten or fifteen minutes in having tables provided for late arrivals.

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## OBITUARY

Bryce Washington Fontaine (Fellow), Memphis, Tenn., died March 31, 1929, aged 51.

Dr Fontaine received his medical degree from the University of Texas School of Medicine in 1896 and from the University of Pennsylvania School of Medicine in 1897. He pursued postgraduate study at the Harvard Postgraduate Medical School, Johns Hopkins Postgraduate School of Medicine and at the University of Munich. He was Associate Professor of Medicine at the University of Tennessee College of Medicine from 1912 to 1920 and Visiting Physician to the Baptist Memorial and the Memphis General Hospitals during the same period. He was a member of the Nu Sigma Nu medical fraternity, a member of his county and state medical societies, a Fellow of the American Medical Association and a member of the American Climatological and Clinical Association, American Gastroenterological Association, and one of the founders of the Southern Medical Association. Dr Fontaine had distinguished himself in the field of Internal Medicine, not only locally, but nationally, and though only elected to Fellowship in the American College of Physicians one year preceding his death, his influence and his participation in College affairs will be regretfully missed.

Joseph William Rowntree (Fellow), Waterloo, Iowa, died April 3 1929, of heart disease following influenza and diabetes, aged 50 years

Dr Rowntree received his degree of Doctor of Medicine at the Trinity Medical College, Toronto, Ontario, Canada, in 1903 and pursued post-graduate study at the Mayo Clinic and at the Johns Hopkins University School of Medicine. From 1915 to 1917, he was Lecturer on Roentgenology at the Rush Medical College, Chicago, and head of the Department of Roentgenology at the Presbyterian Hospital. Since 1917, he had been a Roentgenologist and Pathologist at the St Francis and Presbyterian Hospitals of Waterloo. Dr Rowntree was a member of his county and state medical societies, a Fellow of the American Medical Association and a member of the Radiological Society of North America. He has been a Fellow of the American College of Physicians since December 30, 1921

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Arthur Solomon Loevenhart (Fellow), Madison, Wisconsin, died April 19, 1929, at the Johns Hopkins Hospital, Baltimore, Maryland, following an operation for gastrojejunal ulcer.

Dr Loevenhart was born at Lexington, Kentucky, December 29, 1878, attended the Kentucky State University, from which he received his Bachelor of Science degree in 1899 and then attended the Johns Hopkins University, from which he received his degree of Doctor of Medicine in 1903. From 1903 to 1908, he served in various capacities on the faculty of his Alma Mater, teaching in the Department of

Chemistry and Pharmacology. In 1908, he became Professor of Pharmacology and Toxicology at the University of Wisconsin Medical School, which position he held until the time of his death. During the World War, he was Chief of the Section on Pharmacology and Toxicology of the Research Division of the Chemical Warfare Service, and since 1920 had been a Consultant to the same Service.

Dr Loevenhart was a member of the Phi Beta Pi, Phi Lambda Upsilon, Phi Beta Kappa, Phi Kappa Phi and Sigma Xi fraternities. He was also a member of his county and state medical societies, the American Medical Association, the American Physiological Society, the American Society of Biological Chemists, the Society for Experimental Biology and Medicine and an ex-President of the American Society for Pharmacology and Experimental Therapeutics. He had been a Fellow of the American College of Physicians since December 30, 1926.

His contributions approximately sixty, in the fields of Pharmacology, Chemistry, Physiological Chemistry and Therapeutics acquired widespread attention. It is said that his department of the University of Wisconsin was especially productive of many "brilliant students and investigators."

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title was decreed to Dr Sajous in 1893 (The surname, Sajous, by which he was known is that of his step-father, James Sajous, which was assumed to comply with the necessities of certain inheritance laws in this country)

Dr. Sajous attended school in Paris for a number of years and then coming to the United States he began the study of Medicine in the University of California. Later he transferred to the Jefferson Medical College where he received his M D degree in 1878.

Doctor Sajous was one of the first practitioners in Philadelphia to limit his professional work to diseases of the nose and throat in which field he gained a well deserved reputation as a skilled and learned specialist. Dr Sajous was a true scientist and refused to narrow his scientific interests to any restricted field.

He was Professor of Anatomy and Physiology at the Wagner Institute of Science from 1880 to 1882, Lecturer upon Laryngology at the Jefferson Medical College from 1881 to 1890. During 1897 and 1898 he was Dean and Professor of Laryngology at the Medico-Chirurgical College of Philadelphia and from 1910 to 1922, he was Professor of Therapeutics at Temple University School of Medicine, Philadelphia, and from 1921 to the time of his death he was Professor of Endocrinology at the Graduate School of Medicine of the University of Pennsylvania.

Dr Sajous received the degree of Doctor of Laws from St Joseph's College in 1909 and the degree of Doctor of Science from Temple University in 1915.

Early in his professional life, he

formed the habit of continuing his scientific studies and researches abroad. He was fortunate in working with Brown-Sequard in Paris and became greatly interested in the nature and function of the ductless glands.

Dr Sajous has long been known as "The Father of Endocrinology." He was not only one of the earliest workers in this field of endeavor but his continued interest, publications and presentations gained for him a worldwide reputation as one of the foremost authorities upon endocrinology.

Dr. Sajous was the author of numerous articles and books, among the latter are "The Internal Secretions and the Principles of Medicine" and "Sajous' Annual and Analytical Encyclopedia of Practical Medicine." He was editor of the New York Medical Journal from 1911 to 1919.

Dr Sajous was a member of the Philadelphia County Medical Society, The Pennsylvania State Medical Association, The College of Physicians of Philadelphia, ex-president of the American Medical Editors Association, ex-President of the American Therapeutic Society, ex-President of the Association for the Study of Internal Secretions, a member of the Association of American Physicians and had been a Fellow of the American College of Physicians since December 1916. He was a Member of the Legion of Honor of France and Knight of the Order of Leopold of Belgium.

Dr Sajous impressed strangers as well as those who knew him well with his truly distinguished appearance. There was no likelihood of mistaking him for other than a physician. A noble bearing as befitted his birth, a

gentle, considerate and thoughtful men, courteous and kindly in all his acts, encouraging and inspiring to younger colleagues—in truth one of Natures' noblemen Dr Sajous will be remembered pleasantly by all with whom he came in contact

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### JOHN ALEXANDER WITHER- SPOON

In the death of John Alexander Witherspoon (Fellow 4/3/22) at his home in Nashville, Tennessee, April 28, 1929, the medical profession of America lost one of its most outstanding members Born in the rural districts of Tennessee, Dr Witherspoon after a rural school education and a year of work in Austin College, Texas, studied medicine in a physician's office for two years and then entered the University of Pennsylvania from which he was graduated in 1887 with honors He returned to Columbia, Tennessee to engage in practice, but his unusual ability and personality soon caused him to be called to the University of Tennessee College of Medicine at Nashville where he filled the chair of physiology and later became professor of medicine until 1895

When the Medical Department of Vanderbilt University was established in 1895 Dr Witherspoon became professor of medicine and for thirty-three years served in this capacity and that of clinical professor of medicine To Dr Witherspoon more than to any other individual is due credit for the present position of this school

Through long years of untiring service he was able to organize the framework of a great institution and, though for years handicapped by lack of adequate funds, through his energy, vision and devotion to teaching he became the real influence which secured aid from philanthropic agencies, making possible the erection and maintenance of the present new buildings

During his entire career Dr Witherspoon was active in medical organization work and in an effort to improve the profession and to raise the standards of medical education He joined the American Medical Association in 1890 and in 1904 was appointed a member of the Council on Medical Education and served in that capacity for nine years He was elected a vice president of the Association in 1902, a member of the House of Delegates in 1922, 1924, 1926, and 1928, and President of the Association in 1912 During his administration he was a delegate to the International Medical Congress in London, and in 1909 was appointed by Secretary of State Knox to deliver the acceptance address during the International Congress of Medicine in Budapest at the dedication of the statue to George Washington He received the degree of doctor of laws from the University of Georgia in 1913 Dr Witherspoon was a Fellow of the American College of Physicians, editor of the Southern Medical Association

Association and the Southern Medical Association.

Some men are blessed with intimate friends and others with great numbers of acquaintances. Dr. Witherspoon had both—his ability, integrity, courage, fairness and affectionate nature binding firmly to him those with whom he came in close contact, while his genial nature, his sense of humor and his unusual ability as a speaker made him widely known to the profession and laymen in general. To his students he was not only a great teacher, but an intimate friend as well, always ready to lend a helping hand in the solution of problems of student life. To all of these—friends, acquaintances, students—his passing has left a void difficult of being filled, but his memory will remain as an inspiration in years to come to those who knew and loved him.

(Furnished by Dr. J. Owsley Manier, Nashville, Governor for the State of Tennessee.)

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Frank Cornelius Balderrey, Tucson,

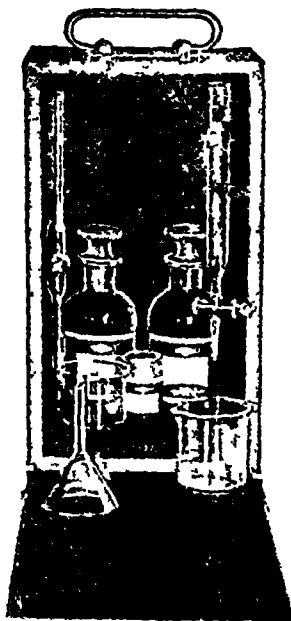
Arizona, one of the recent Fellows elected during the Boston Clinical Session, in April, 1929, died May 9, following an operation, aged forty-two years.

Dr. Balderrey received his medical degree from the University of Illinois, College of Medicine, Chicago, in 1913, and his internship was spent in the U. S. Marine Hospital of Detroit; thereafter he became Senior Resident at the Seton Hospital, New York City, and Medical Adviser to Cornell University. Following this he was Director of Research at the J. N. Adam Hospital, at Perrysburg, N. Y., and still later Associate Medical Director of the Desert Sanatorium, at Tucson, Arizona. During the World War, he was a Lieutenant in the Medical Corps of the U. S. Army. He was the author of a number of articles dealing with Heliotherapy.

Dr. Balderrey was a member of the Pima Medical Society, the Arizona State Medical Society, the American Medical Association, and a Fellow of The American College of Physicians.

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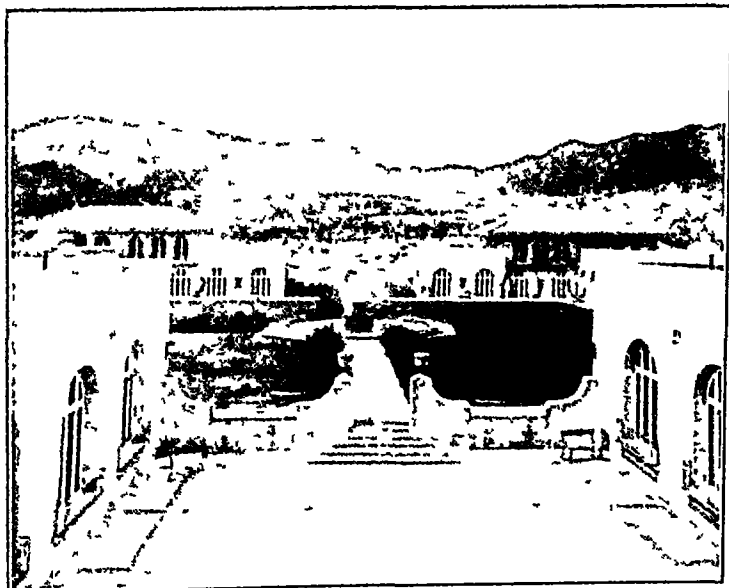
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The Journal will make an especial feature of the reviews of monographs and books bearing upon the field of Internal Medicine. Authors and publishers wishing to subject such material for the purposes of review should send it to the editor. While obviously impossible to make extended reviews of all material, an acknowledgment of all matter sent will be made in the department of reviews.

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ALFRED SCOTT WARTHIN, M.D.  
Pathological Laboratory, University of Michigan  
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A NEW MACMILLAN PUBLICATION

# THE CLINICAL ASPECTS OF VENOUS PRESSURE

By

J. A. E. Eyster, B.Sc., M.D.

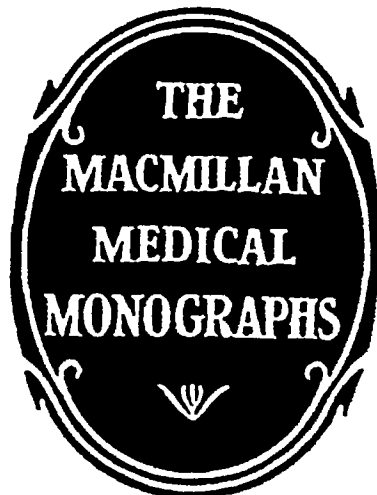
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Cloth, 8vo, 135pp., \$2.50

This book is written primarily for the clinician, and stresses the clinical application of venous pressure. Since an understanding of normal conditions must precede the interpretation of abnormal states, a brief review and presentation of the present conception of the cause and significance of venous pressure is given, followed by a discussion of the altered state that exists in cardiac decompensation. The conception of this condition, which is presented in many of its details, has come only recently through a more thorough understanding of cardio-dynamics, especially in its relation to venous pressure. Following this the method and its clinical applications are discussed. A bibliography covers quite fully all literature on this subject up to the present time.

The author states in his introduction

"Venous pressure may be said, therefore, to represent not only the primary factor that underlies the symptoms and functional pathology of cardiac failure but is also responsible in large part for the physical signs accompanying it—edema, congestion, cardiac dilatation, and reduced urine secretion. As the principal underlying factor in these conditions, and as the principal index of cardiac behavior, it is the most reliable and important single factor to know and to follow accurately when this clinical state develops or when it is impending."



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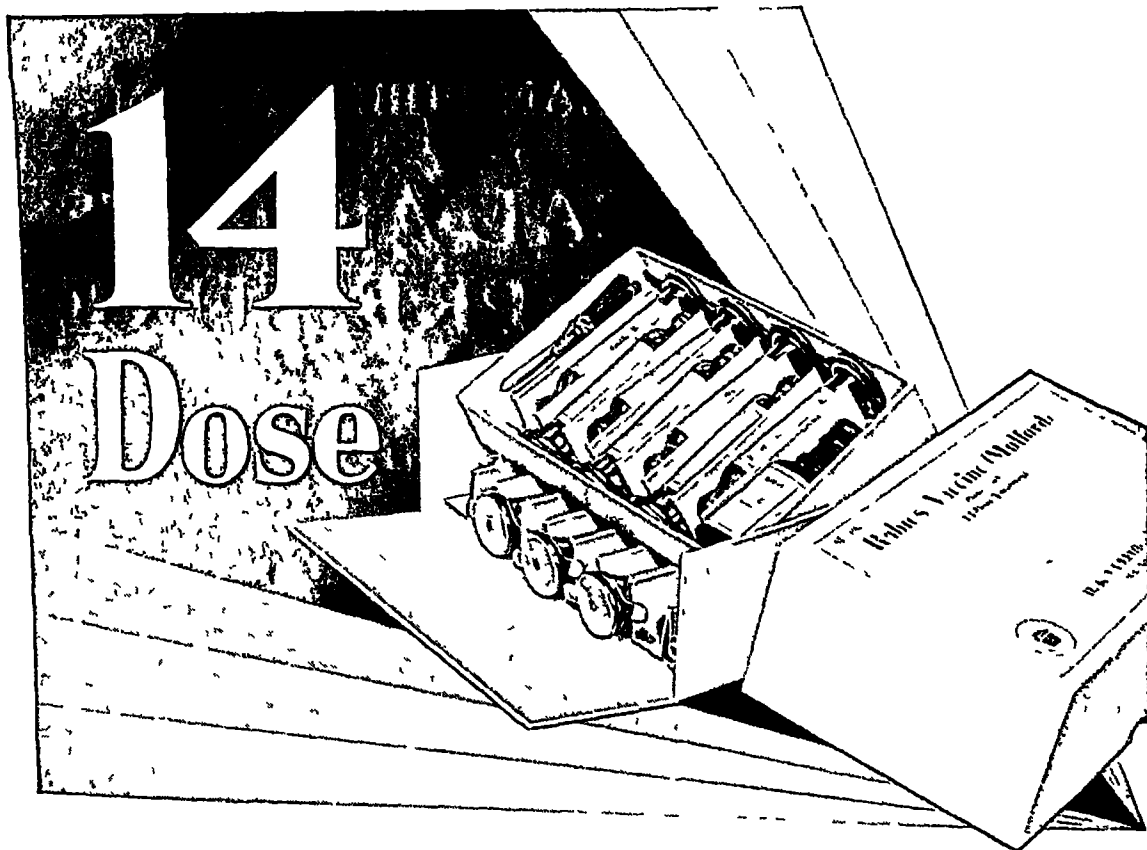
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# Atypical Features of Acute Coronary Occlusion\*

By JAMES B. HERRICK, *Chicago, Illinois*

WHEN I asked Dr Means, our General Chairman, if the subject of acute coronary obstruction were not already old and well worn especially in Boston, he replied that he did not think the problem of coronary obstruction had been worked to death in the east. "The patients have died but not the subject which is ever present and very important." So, with this diplomatically worded official encouragement I venture once more to present this topic.

Acute coronary occlusion was formerly regarded as a pathological curiosity. It is now looked upon as a readily recognizable clinical entity of rather frequent occurrence. I am often asked whether the condition is more common now than it used to be. It is difficult to answer this question positively. Some writers think thrombosis in general is more common than formerly. Probably the seemingly greater frequency really means more frequent recognition both by clinicians and pathologists.

One reason for this belief is that as one reviews the literature one is surprised to find how many cases were described many years ago. In 1910 there were published three outstanding articles on this subject but they at-

tracted little notice. Obratzow and Strascheko clearly described the clinical features showing the possibility of diagnosis during life. They emphasized the status anginosus, and called attention to the resemblance to abdominal surgical affections. Osler's accurate observations were largely lost because the condition was described as an incident in, or a variant form of, angina pectoris. Sternberg's monograph on Partial Aneurysm of the Heart is filled with histories of cases but the emphasis is on the later so-called aneurysmal effects and little attempt is made to depict the clinical onset of the condition. In the same way the earlier masterly work of René Marie on Infarct of the Myocardium, in 1897, was chiefly a contribution to pathology. The reason no more marked impression was made by these papers and by others that preceded them was because the cases were viewed as rarities, as nearly always resulting fatally and as almost impossible of intra vitam diagnosis, or they were approached from an entirely different avenue than the clinical.

But in the last two decades pathologists and clinicians—and American observers have played a conspicuous part—have paid more attention to the coronary artery have more carefully analyzed cases of angina pectoris,

\*Read at the Boston meeting of the College of Physicians, April 10, 1927.

acute dilatation of the heart, heart failure, ptomaine poisoning and acute indigestion, and the importance of obstructive lesions in the coronary artery has been recognized and the clinical features more clearly depicted

It has often happened that the earlier views concerning a disease have had to be modified as time went on and experience broadened. The clinical picture of exophthalmic goiter of thirty years ago is not that of today, particularly with the help offered by the basal metabolic rate determination. Mild, atypical, bizarre cases are today recognized as associated with faulty thyroid function that then would have been passed as not fitting into the classic syndrome of symptoms. In a similar way our conceptions of acute coronary occlusion are being gradually modified and will be still further altered, for our knowledge of it is far from complete both as to etiology, pathology, clinical manifestations, prognosis and treatment.

In this paper I desire to call attention briefly to a few atypical features of this condition.

By the typical picture is understood something like the following:

The patient, generally an adult who may have known of hypertension or may have had angina pectoris, is seized suddenly, perhaps while quiet, with a severe substernal or upper epigastric pain that may radiate to the neck, arms or epigastrium. Contrary to the rule that holds in attacks of angina of effort the pain does not soon disappear, it lasts and requires large doses of morphin for its relief. There is evidence of shock or collapse, the countenance is ashy, the pulse weak, gen-

erally rapid, perhaps irregular, the heart tones faint. The blood pressure falls. Dyspnea may be marked. Death may occur in a very short time or the patient may live days, weeks, or may recover. The heart may show that it has been hard hit, by its persistent weakness or irregularity and by dyspnea, râles, enlarged liver, albuminous and scanty urine. Strongly suggestive are a pericardial friction a few hours or days after the accident due to the roughening of the pericardium over the infarcted area; also a rise in temperature and a leucocytosis. Electrocardiographic changes are quite significant. Such a grouping, when other diseases that might produce similar symptoms can be excluded—such as gall-stones, perforating ulcer, acute pancreatitis, diaphragmatic hernia, pneumothorax—is almost pathognomonic of acute obstruction of the coronary artery.

But not all cases are so classic. In 1912 when I first became interested in this subject I made a tentative grouping as follows:

- 1 Cases of instantaneous death
- 2 Cases of death in a few minutes or hours
- 3 Cases of severity, with death deferred for many hours, days or weeks, or at times ending in recovery, i.e. the cases that live long enough to permit of study and that arouse the greater clinical interest. The type of this case I have just described.

#### 4 Cases with mild symptoms

This latter group I am convinced is far more important than is generally realized. There are, to quote from

what I have written elsewhere<sup>1</sup> "non-fatal cases with mild symptoms, slight anginal attacks, perhaps without the ordinary causes such as walking. Some of the stitch pains in the precordia may well be due to obstruction of small coronary twigs. Such interpretation of these phenomena, while largely a surmise, is based on the fact that other causes for the pains are lacking and that the patchy fibrosis of the myocardium that is later found at autopsy may have originated in a progressive narrowing of the sclerotic vessels, with, from time to time, acute thrombotic occlusion of small branches, and such obstruction in small vessels may well have produced symptoms differing chiefly in degree from those caused by obstruction of the larger arteries of the heart. Since 1912 when I began looking for these cases of coronary obstruction clinically, I have seen several patients in whom I have felt that such obstruction of small vessels with mild symptoms had occurred. In some instances two or three attacks of mild character differing from the more familiar effort paroxysm of angina pectoris have been followed at some later period by severe and unmistakable symptoms of occlusion of a vessel of larger size. A thrombus in a small branch of the coronary artery may produce mild symptoms just as a clot in a small twig of the cerebral vessels may cause transient and comparatively trifling symptoms very different from the hemiplegia or possibly sudden death that follows the embolic

or thrombotic plugging of a vessel more important or of larger size."

Many such cases never come to the doctor, the distress and disturbance are so slight as to be ignored by the patient. Other cases are easily overlooked even when the doctor examines carefully. Breathing, color, heart rate, heart tones, blood pressure etc., may be apparently unchanged. In some it may be suspected that a coronary accident has occurred, especially if blood pressure can be shown to have fallen a few points, if there be a slight elevation of temperature or increase in polynuclear white blood cells or if the electrocardiogram shows suggestive tracing.

Under this head may perhaps be included attacks when the pain is frankly substernal, quite severe, with short-lived fall in blood pressure, perhaps extrasystoles with slight elevation of temperature, but in which in forty-eight hours there is an apparent return to normal, no dyspnea, pain or heart irregularity, no fever with the patient insisting on getting up. He has seemingly recovered.

But some of these apparently mild cases are deceptive and treacherous. A doctor on the third day got up, walked on the street, suddenly dropped dead apparently from ventricular fibrillation. The autopsy showed the obstructing thrombus in the descending branch of the left coronary artery. A woman a few days after a cholecystectomy for gall-stones complains of slight pain in the arms, has dyspnea, rapid pulse with extrasystoles. In three days she seems better in all respects, dresses her hair herself, laughs and jokes with the surgeon. She is left at ten o'clock

<sup>1</sup>The Weekly Roster and Medical Direct of The Philadelphia County Medical Society, May 23, 1925, p. 15.

at night sound asleep, breathing easily. At one A.M. she is found dead lying on her pillow in an easy position on her side, one arm under her head. A recent thrombus in the descending branch of the left coronary, acute infarct of the myocardium with rupture of the ventricle tell the story.

Some of the patients who have these mild attacks ending in recovery have moreover recurrences in a few days, months or years. Either the thrombus has extended proximally or new thrombi have formed in other vessels.

In most of the descriptions of acute coronary occlusion, pain, usually sudden, is described as an outstanding feature, a pain resembling that of angina of effort, yet often more severe and more persistent, frequently referred to the lower sternal region or to the epigastrium. That this pain should differ in intensity and other characteristics depending on the vessel occluded, its size, e.g. right or left coronary, descending or circumflex branches, or smaller branches,—upon the suddenness or the completeness with which the artery is plugged, is to be expected. So, also, the condition of the coronary system as a whole might materially influence not alone the extent of the infarcted area but the degree of pain experienced. A coronary vessel in which sclerotic changes have been going on for a long time, is often better able to withstand the sudden occlusion because in a compensatory manner collateral vessels have been enlarging as the lumen of the artery in question has been gradually narrowing. Paradoxical as it may seem, a heart with relatively normal coro-

naries may be less fitted to withstand the insult of a thrombotic closure than the one whose vessels have long been the seat of extensive sclerotic changes. Varying degrees of pain, therefore, might be anticipated because of these varying anatomic conditions present in the heart affected. Such is the case. From the severest pain that resists even large doses of morphine and that lasts for hours or perhaps days throughout a period of status anginosus the pain shades down to milder and milder types until we find instances where there is no pain.

While in my own experience some pain has nearly always been present and generally has been severe, many observers call attention to cases where pain has been absent. Sudden dyspnea, with symptoms of collapse, clammy sweat, nausea, ashy color, and definite drop in blood pressure speak for a cardiovascular accident. The subsequent history showing perhaps a pericardial friction, rise in temperature, leucocytosis, with persistent evidences of cardiac weakness, with typical electrocardiogram tend to confirm the impression of coronary occlusion. Autopsy reveals the obstruction with the myocardial changes. Some regard a suddenly developing dyspnea as a phenomenon more significant than pain. Others stress the abrupt drop in blood pressure. Dyspnea and drop in blood pressure might be spoken of as the pain equivalents of acute coronary occlusion. Is it not better to look upon the *grouping* of symptoms as the surest indication of the accident rather than to overstress the one?

Gallavardin and Gravier<sup>2</sup> regard pain—referring to it as *angina pectoris*—as playing a secondary rôle in the symptomatology of cardiac infarct. One reason for their view which differs from that of most other observers, is that they are considering not alone the cases of acute coronary obstruction but subacute and chronic as well.

It is clear that we should not stress the symptom of pain too much. We should not, because pain is slight or even lacking, exclude occlusion when other symptoms point to this accident.

Sudden dyspnea has been stated by some to be the regular, invariable accompaniment of this condition. It is of common occurrence. But in some cases it is trifling or entirely lacking. Râles, cyanosis, Cheyne Stokes' breathing, dyspnea, while often present are very variable as to frequency, degree, and time of appearance. They largely depend, one must assume, on the extent to which the heart's efficiency, especially that of the left ventricle, has been interfered with. The easy breathing of some patients whose rapid pulse, feeble heart tones and low blood pressure show marked cardiac weakness has sometimes been a surprise.

More careful and extended observations with post-mortem check may enable us to explain why in some instances dyspnea is marked and in others not. It is to be recalled that some authors e.g. Pletnew and Libman have already aimed to distinguish between an infarction in the right heart and one in the left. According to them dyspnea is more outstanding

when there is damage to the myocardium of the left heart.

A marked drop in blood pressure is very significant. Such a drop is particularly helpful in diagnosis when the existence of a previously high pressure is known. But I have seen cases in which the pressure stood up wonderfully well. And another puzzling feature in some instances has been the remarkable daily variations in pressure—a systolic pressure today of 120, tomorrow of 180, etc.

Perhaps after all, these variations are no more to be wondered at than are those of the pulse. Commonly rapid, weak, perhaps with extrasystoles, it may be full, regular, not rapid, or it may show extrasystoles, block, auricular fibrillation. And most extraordinary variations are possible from day to day or even from hour to hour.

One might dwell on other atypical features. Some cases have little or no rise in temperature or even a sub-normal temperature. The leucocytes may vary much in number. The radiation of pain may be as variable as in angina of effort. The electrocardiogram may show most remarkable and bizarre pictures with almost unbelievable variations from day to day. The close resemblance of many cases to surgical abdominal accidents has been dwelt upon by many writers. The differential diagnosis is generally easy if this cardiac condition is thought of; but not always. One may at times feel that it is wiser to have an exploratory operation to remove the doubt than to await developments, perhaps by waiting taking from the patient his only hope of recovery by operation. The instructive case recorded by McNee

<sup>2</sup>Gallavardin et Gravier. *Formes Cliniques de l'Infarctus du Myocarde*. *Annales de Med.* 1926 Sep., p. 161.

might be cited as a good example. Especially difficult are those cases in which an individual has, let us say, gall-stones or duodenal ulcer and then has an acute coronary occlusion. I know of one instance where in such a case the patient died suddenly during the operation for gall-stones, the autopsy revealed a recent infarct of the myocardium and rupture of the heart. The gall-stones also were there. Which had caused the initial symptoms?

There is only one other point to which I will call attention, though many others might be mentioned. There is a general agreement that the obstruction in these acute cases while occasionally due to an embolus, is usually caused by a thrombus that forms *in situ*. But in a not inconsiderable proportion of cases embolic phenomena are noted after the accident, at times soon after, at other times many days or even weeks later. The explanation commonly offered is that from the intracardiac thrombus that forms over the site of the infarcted area fragments may be detached and lead to the embolic obstruction of peripheral arteries. If the embolus springs from the right heart the pulmonary artery may be obstructed.

There is another possible explanation for some cases, viz multiple arterial thromboses. This question deserves further investigation by clinicians, pathologists and experimental workers. The damage to the vessel walls that favors the formation of a thrombus, i.e. the arteriosclerosis and atheromatosis, may be widespread and not limited to the coronaries. There is reason to believe that infection

with acute arteritic changes may be a contributing or even determining factor in producing the obstructing thrombus. Unrecognized qualitative or quantitative chemical changes in the blood, or in the number of platelets may be contributing factors. It is conceivable therefore that conditions in the blood with widespread chronic and recent acute changes in the vessel wall may account for the appearance of thrombi not only in the coronary arteries but in others as well. The same question has caused discussion as to the origin of postoperative pulmonary infarction. Generally regarded as embolic, there are those who view the accident as in many instances due to local thrombosis in the pulmonary arteries.

Whatever the explanation in these cases of acute coronary occlusion—and the embolic theory is the best working theory and has much presumptive evidence in its favor—the clinician must be prepared to meet from time to time with evidences of obstruction in other vessels. Emboli in the brain, the kidney, the spleen, the vessels of the leg are occasionally seen—though in my experience rather infrequently. One of the most distressing deaths I have ever witnessed was in a man of sixty with preceding angina of effort, with acute coronary obstruction and the status anginosus. A few hours before death he had most excruciating pain in one leg with disappearance of pulsation in the artery. In another case there was what we regarded as an acute mesenteric obstruction. Hamman has recently reviewed this feature and cited several instructive cases.

The summary of this fragmentary paper is that our picture of acute coronary occlusion must not be drawn with too fixed lines. We must allow for many variations from the ordinary type, for mild and subacute cases, for cases without pain, for instances of extreme variation in blood pressure, degree of dyspnea, temperature, pulse rate and rhythm. We must be pre-

pared as well for cases with early or late embolic accidents, for recurrences due to proximal increase in the thrombus or to involvement of new vessels. If all this is done the condition will be recognized more frequently even than now and probably a larger percentage of deaths from angina pectoris will be shown to be due to this accident in the coronary artery.



# The Failing Heart of Middle Life\*

By DAVID RIESMAN, M D , Sc D , *Philadelphia*

MANY men lead active professional and business lives, they may even live reasonably well according to our present standards, but when they reach the age of 50 or thereabouts something happens that was not foreseen by them or by their medical advisors. In ordinary parlance they go to pieces. Upon analysis the disintegration will usually be found due to some change in the heart or circulation. The man who up to the moment of the appearance of the symptoms was active and in the possession of all the energy of the best years of life suddenly becomes an old man.

What is the nature of this process which plays such havoc among useful men, more rarely among women, and in a time of life that we like to call the prime? To be sure there is no definite agreement as to what should be called the prime of life or middle life—youth sets the date early, age postpones it. One day not long ago a student presenting a case before my class began, "Mr. X is a middle-aged man of 40." My heart sank within me. Does middle life begin at 40 or at 50 or, as I like to think, at 55 or 60, partly with reference to the fact that the average span of life has been pro-

longed to about the age of 56? Women surely are pushing the date farther and farther onward—in dress, in general activity, even in the onset of the menopause, the women of today at 50 are much younger than their mothers were at the same age period. Perhaps instead of taking a particular year, middle life should be dated from a time when a change in function manifests itself from which a beginning wearing down of the machinery can be definitely inferred. Middle life is thus rather a physiologic than a chronologic period.

The disease of the heart to which in the majority of cases the physical breakdown is due is not one affecting the valves—it is as Christian has called it, non-valvular heart disease. Whatever we may know about the clinical manifestations, as to the causes of this condition we are very much in the dark. Sometimes there is an associated hypertension which may be looked upon as the cause. But since we do not know much about the causes of hypertension we are only pushing the problem one step farther back. In other instances the tension is normal or even low. In such cases the changes are usually primary in the heart—a coronary endarteritis or, more often than we think, some functional

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change for which at present we have no anatomic substratum

Like Christian (*South Med Jour*, Jan 1927, p 28) I have stood more than once in perplexed wonder at the autopsy table when I found an apparently normal heart in a case in which death had been due to cardiac failure. The converse was also not unusual, namely, the finding in a case of accidental death extreme disease of the heart wall though during life there had been no symptoms whatever of a cardiac nature. Such observations prove conclusively that the diseased heart often possesses large factors of safety and suggest that the symptoms are expressions of functional disturbances rather than of anatomic defects.

Failing heart and heart disease are convenient terms, but in their strict meaning they are not sufficiently inclusive. They are largely anatomic concepts—the time has come for a more physiologic interpretation of heart failure. Our conception of the failing heart must encompass the whole circulatory system, including the capillaries. It must also include those obscure metabolic changes arising from defective circulation in the organs and especially in the body musculature.

Some insight into the physiologic disturbances accompanying, or produced by heart disease is gained through recent biochemical and metabolic studies. Among other things these have shown that in many cases of heart disease there is an increase in the minute-volume of blood and that with improvement, especially under the action of digitalis, there is a diminution of the total circulation, of the minute-blood volume (Harrison and Leon-

ard, Cohn and Stewart). It has been found, furthermore, that owing to an oxygen deficiency in cardiac cases more lactic acid is formed than under normal conditions. While in health a large part of the lactic acid is resynthesized to glycogen, in diseases of the circulation a good deal of the lactic acid formed undergoes destruction by conversion into carbon dioxide and water which entails a distinct loss to the system. Owing to the increased lactic acid production cardiac cases at times present a tendency to acidosis which shows itself in a highly acid urine and in a lowered urinary pH and which may be responsible for certain forms of cardiac dyspnea. To what extent the heart as muscle tissue participates in the altered lactic acid metabolism is not yet known. Many cardiac cases also show a high basal metabolic rate.

The great increase in deaths from heart disease is I believe due to the type of middle life myocardial failure of which I am speaking. Disease of the heart has risen to first place in mortality tables. The Metropolitan Life Insurance Company's statistics for 1928 show a death rate of 143.4 per 100 000 insured while that from tuberculosis was exactly 90, the lowest ever attained. This marks a drop in tuberculosis of 34.7% during the present decade while the death rate from heart disease has risen from 117.4 in 1921 to the above-mentioned figure. In the United States Registration Area the cardiac mortality was 111.2 per 100 000 in 1910 and nearly 160 in 1924.

To a certain degree the increase in death rate from heart disease is due

a debit but a credit, since owing to the enhanced longevity and to the fact that fewer persons die of tuberculosis and other communicable diseases, more individuals reach the age period at which the liability of death from heart disease attains high figures. Nevertheless there is also an actual increase irrespective of the foregoing facts. It is this increase that should be investigated and combated by education of the people and of the medical profession.

When we come to look for the causes of myocardial disease we find certain outstanding facts which while not precisely explanatory of the cause throw considerable light upon the origin of the trouble. Syphilis and rheumatic fever in my experience play only a small part in the myocardial disease coming on at middle life. Worry, overeating, sexual excess, intense ambition and striving for success, in other words, the strenuous life, are antecedent conditions.

Not only overeating, but irregular and hasty eating, and insufficient sleep are important etiologic factors, especially in the lives of professional men. Focal infection in all probability plays a rôle but it is difficult in the majority of cases to trace a direct connection because when a focal infection is discovered it has probably been operative so long that its removal though indicated has but little effect. The conclusion is likely to be drawn that the focus played no part in the development of the cardiac disease.

Over-indulgence in exercise is undoubtedly a cause of cardiac damage. There are many whose economic circumstances in early life precluded sys-

tematic exercise, but when they get to be 45, 50, or older then are in a position to indulge in golf—some do so with impunity, others pay a heavy penalty. Men who want to take up golf in middle life ought not to do so without a thorough physical examination which ought to be repeated after they have played a little.

The various exciting causes that I have enumerated are operative in the majority of Americans that have reached the mid-period of life. Why do they not all succumb to myocardial or cardiovascular disease? Because something else is required—an underlying condition which is given in a large number of cases by heredity.

*Heredity* During the past ten years there has been an evident swing of the pendulum away from the environmental factors in disease, including the micro-organismal agents, toward the constitutional factors. Some perhaps are permitting the pendulum to swing too far but no one who has practiced medicine with an open eye can overlook the fact that the bacterial or other environmental influences are scarcely sufficient by themselves to cause disease, barring of course trauma and semi-traumatic agents, such as poisons and harmful dust.

During the period when Philadelphia was one of the worst typhoid-infected cities in the land, a period coinciding with my early years in practice, I was struck by a singular circumstance in two families of my acquaintance. Nearly every member of the one at some time had typhoid fever, while in the other family, comprising individuals in a number of separate households, there was not a single case of

typhoid fever, although the same contaminated drinking water was consumed by all. That observation it seems to me warrants the conclusion that a constitutional factor protected the second family, that factor being absent in the first, or to put it another way, the members of the typhoid family inherited from generations back a high susceptibility.

Now when we come to study myocardial disease or diseases of the circulation a somewhat similar fact emerges. We find families that seem to be entirely or almost entirely immune to mid-life circulatory diseases. I have gathered statistics of a family related to me by marriage—in two generations there were 56 members all born in Philadelphia and belonging to several different households. Of the 56, 11 have died, not one of myocardial disease. Those living range in age from 40 to 85 years. By contrast I know a family in which two out of four have died of angina pectoris, in another of five members one has died of angina pectoris, another is seriously ill with coronary disease.

The familial circulatory taint need not assume the identical form—it may be angina pectoris in one, coronary thrombosis in another, apoplexy in a third, and ordinary myocardial degeneration in a fourth. When such related diseases affect the same family we are warranted in inferring that a constitutional anomaly exists, a taint of the genotype without which whatever external factors may exist are inoperative or at least incapable of doing the same degree of harm. I shall today not enter into the possible anthropologic features that might lead to a recogni-

tion of the abnormal genotype. George Draper, Julius Bauer, F. Kraus and others have indicated the pathways to be followed in this difficult field. What I want to emphasize is the importance of a study of the family history. It will be found that short life is as much an hereditary trait as longevity, which is undoubtedly a family characteristic. That there are exceptions in any given family does not disprove the truth of the statement. I am sure the myocardial disease of middle life of which I am speaking is preeminently a familial or hereditary affair, a fact of which anyone can convince himself by studying the family trees of his patients.

Obesity is another possible etiologic factor. I am not sure whether my experience tallies with that of other men, but I have come to believe that the hydrolipemic type, the excessively fatty individual, does not as a rule fall a victim to presenile myocardial disease. It is the overweight solid type, men and women whose fat is firm, who are not very far above the ideal weight, not grotesque in their obesity, among whom we find myocardial disease most frequent. It can not however be said that there is a characteristic physical type liable to myocardial disease. All physiques are met with, the tall and lank, the shortnecked and solid.

*Pathology.* The actual pathologic conditions vary widely and are, as I have indicated at times, disproportionate to the symptoms during life. Eppinger reports two cases that are of interest in this connection. Both had advanced decompensation, in one the heart at autopsy was markedly dis-

eased, in the other very little could be found.

Many use the term myocarditis for the diseased condition I am discussing. In a strict sense that word is not always applicable, for the criteria of inflammation are frequently wanting. We meet with the same complication in our nomenclature of kidney affections. Because of the similarity of concepts and of morbid states, I believe we might use the terms myocarditis and myocardosis as we use those of nephritis and nephrosis.

The distribution of myocardial disease is often more important than the type. When it attacks the conductive system, it may produce striking conditions out of proportion to the extent of the lesion. In many instances, in more than is usually imagined, the basis of myocardial disease is an endarteritis of the coronary vessels.

*Symptomatology* Patients with myocardial disease present, in the beginning at least, four principal types of symptoms that might be called

- I The respiratory.
- II. The digestive
- III. The painful
- IV The oppressive

The respiratory is the most common type. An individual previously well, perhaps fifty or fifty-five years old, experiences shortness of breath on effort or he finds himself seized with paroxysms of air hunger, especially at night, which compel him to sit up and gasp for breath. I have seen this latter type as the very first manifestation of serious structural disease of the heart, in the entire absence of any valvular defect or of any previous suspicion

that the heart might be diseased. The patient, and sometimes the physician, attributes the shortness of breath to lack of exercise, to obesity, to indigestion, the last especially if there is considerable gaseous distension. A careful examination in the way I shall later detail will guide the physician to the vitally important correct diagnosis.

Sometimes in addition to a slight shortness of breath the myocardial patient has a racking cough usually out of proportion to the signs found in the lungs. Such patients are looked upon as having chronic bronchitis or asthma, the myocardial cause being overlooked.

## II The digestive type:

This is perhaps the most important to understand as errors in diagnosis are more frequent than under other conditions. Elsewhere I have spoken of the gastric masquerades of myocardial disease (*Journal of the American Medical Association*, November 17, 1928, Volume 91, 1521). A case report will illustrate this phase of the subject. Mr. T, a successful and somewhat opinionated financier, complained of poor appetite, gaseous distension, constipation and insomnia. His case had been diagnosed as one of stomach and liver trouble and he had been sent to Vichy on the basis of that diagnosis. Under a rigid regime which excluded all meat from the dietary, he lost a good deal of flesh and came back to Philadelphia much worse than he had been. On examination I found a tall spare man of pale sallow complexion with labored breathing, which he said was due to "gas." The heart was markedly enlarged to the left, the liver extended three fingers' breadth below the costal margin. I

placed the patient on a liberal diet and gave him digitalis, a laxative and a mild hypnotic with the result that all his symptoms disappeared, the liver returned to normal size, and he was able about the middle of January to go to Florida

The gastric disturbances are often so marked—anorexia, nausea, even vomiting—that malignant disease may be suspected and yet the whole syndrome harks back to a myocardial defect

Failure to make the proper interpretation is usually due to the absence of a cardiac murmur which needs must be present to induce some physicians to diagnose chronic heart disease. Yet there are more non-valvular than valvular cases of chronic heart trouble

### III The painful type

Little need be said about the anginal type—the pain, in location, severity and psychic concomitants, is usually suggestive or pathognomonic of cardiac disease. Variations occur, however, and require careful study, particularly those in which the pain is referred to the gall bladder region or to the epigastrium. I have seen quite a number of cases in which it was difficult at first sight to tell whether the patient had angina pectoris or gall-bladder colic. It must also be remembered that chronic cholecystitis or gall stone may in its turn cause cardiac disease

Under the anginal type I include coronary thrombosis an increasingly common cause of failure of the heart in middle life. The growing frequency may be due to a better acquaintance with the disease, although I have come to think that there is an

absolute increase in cases of coronary occlusion

### IV The oppressive type

Perhaps it is not justifiable to make a separate type of this, yet it is sufficiently common and distinctive, although it soon merges with one of the others. The patient on walking experiences a sense of oppression either across the upper or midsternal region or in the epigastrium. If he stops it passes off, sometimes with a little belching, sometimes without any gastric element. The trouble appears to be mild, yet it involves the possibility of sudden death. It has been called angina sine dolore but there is no *angor animi* and the patient unless he is a doctor rarely considers the symptom significant

Many persons, especially men of prominence, die according to the newspapers of acute indigestion. The additional statement is often made that the dead man had not complained of heart trouble before. Apart from the probable fact that death was not due to indigestion but to disease of the heart, I always doubt whether the attack was not preceded by symptoms which were of a cardiac nature but were not interpreted either by the patient who failed to have himself examined or by the doctor if an examination was made. To illustrate: Mr S, 54 years of age was passed for life insurance for \$150,000 one month before I saw him in an attack of coronary thrombosis that ended fatally in 48 hours. When the agent came with the policies he brought policies for an additional \$150,000 which the patient declined. Within one month after paying a single premium Mr S was dead.

Now here is the interesting point in the history. It appears that for some time prior to taking out the insurance Mr S had complained of a little mid-sternal oppression unaccompanied by pain. He thought it was indigestion or something of that sort, and as he was not seriously handicapped otherwise, he made nothing of it. His blood pressure, urine, and physical condition during the various insurance examinations were all found normal. Of course, when I saw him, his ashen appearance, his low blood pressure, the terrific pain, and the action of the heart all testified to the approaching dissolution. Could such a catastrophe have been foreseen or suspected as a possibility if note had been taken of the oppressive seizures and a more thorough purposive examination had been made? Would it not be well in all such cases, if the physical signs are negative or equivocal, to make an electrocardiographic examination? I am inclined to think that in such a way the insurance companies may save themselves heavy losses and, what is more important, any defects in the patient's mode of life might be corrected.

Common to nearly all forms of myocardial diseases except the anginal are subnormal temperature, a tendency to emaciation, easy fatiguability and a general lack of mental and physical endurance. These symptoms may be associated with emotional instability and a hair-trigger temperament previously not present in the patient.

Neither singly nor in their totality do the aforementioned symptoms justify a diagnosis of myocardial disease, but they suggest such a possibility even if the signs are not conspicuous.

*Diagnosis* Aside from the symptoms the diagnosis of myocardial disease is based upon the following objective criteria.

The most important is increase in the size of the heart. This is rarely absent. It is determined

a By locating the apex beat by palpation or inspection although this is sometimes impossible because of its faintness.

b By careful percussion of the cardiac outline. While some clinicians have no faith in percussion for the purpose of determining the cardiac boundaries, I personally believe it is a useful method provided a proper technique is employed, namely, light percussion upon a finger held firmly against the chest wall. The X-ray is the final arbiter in this matter.

Auscultation is less informing. In the early stages when the diagnosis is most essential it may show very little to which exception can be taken. But if one carefully examines such cases he may find a dulling of the first sound at the apex or perhaps a treble sound—an apparent doubling of the first sound—the anapest type of gallop. Such a rhythm in a case presenting an otherwise unexplained dyspnea or failure of strength or ill-defined gastric symptoms is to my mind very suggestive of myocardial disease. This particular change in the heart sounds has helped me many times to a correct differential diagnosis as between a purely gastro-intestinal affection and myocardial disease. I want to emphasize that I am not speaking of the gallop commonly heard in mitral stenosis in which the second sound appears to be split or reduplicated, but

of the one which is more like the canter of a horse, or as I have said, the anapest type of gallop

What about arrhythmia?

The significance of this abnormality depends somewhat upon the kind but also upon other factors not always discoverable by physical examination. What I have in mind in this connection is the following. A persistent total arrhythmia is indicative of auricular fibrillation but not every case of this gives a serious prognosis, much depends upon associated conditions, particularly upon the presence or absence of mitral valve disease. I know individuals who have lived for years with a constant total arrhythmia and are leading active lives. There may be a small patch of myocardial disease that upsets the rhythm without in any way disturbing the main functions of the heart.

Extrasystoles may be significant yet there are cases in which extracardiac factors, toxic causes, seem to produce the arrhythmia. The heart behaves otherwise in a normal manner.

The blood pressure has no constant characteristics—it may be high and hypertension is perhaps most common, or it may be normal or low. Usually it falls in the coronary thrombosis cases precipitously, in other cases more or less slowly. A considerable fall in a patient who has no pain but either the respiratory, digestive, or oppressive type of symptoms adds to the gravity of the prognosis.

The electrocardiograph as a rule is very helpful in the diagnosis and in the prognosis of myocardial cases, but it may lead us into error. My experience has been that when the instru-

ment reveals myocardial disease then that disease is present. But when the electrocardiogram is negative a serious myocardial affection may nevertheless exist. I have at the present time under observation three patients in whom the electrocardiogram is normal but in whom everything else points to a definite myocardial damage.

While myocardial disease as such produces no murmur, a murmur may be present, which however in no way vitiates the belief that the disease is non-valvular in origin. Such a murmur is often heard at the aortic area and is transmitted upwards to the clavicles over which it is sometimes heard more loudly with a Bowles stethoscope than over the aortic area itself. This murmur is not due to stenosis of the aortic orifice, it may be due to sclerotic changes in the root or arch of the aorta or to dynamic factors connected with an hypertrophied heart or a dilated aortic arch.

A systolic murmur may also be heard at the mitral valve. Many on hearing such a murmur diagnose mitral disease, mitral insufficiency. That is a wrong interpretation if it implies that the murmur or the regurgitation is due to an old valvulitis. The murmur is a secondary feature of no great moment in the diagnosis but of some importance in prognosis, as it indicates a weakening of the mitral ring or is evidence of extension of the sclerotic process to the valve leaflets.

*Treatment.* When an individual consults his doctor, whether for the purpose of a health examination or for other reasons the physician should carefully go into the family history and estimate the pathologic load upon



the family tree The discovery of an inherited taint, especially of the heart and circulation, should lead to regulation of the man's or woman's life in the direction of conserving the integrity of that system

Foci of infection should be removed if their removal does not entail any undue risk and if a reasonable connection can be conjectured between the infection and the cardiovascular disease

Perhaps the most important point to bring to the attention of the people in connection with myocardial disease is the desirability of regular physical examinations which the profession has been preaching, but so far with not much success The public must realize that to pay for a physical examination in apparent health is money well spent

Treatment must always concern itself not only with the relief of the immediate distress but especially with the prevention of further attacks The primary essential in treatment is rest—physical and mental If the evidence indicates definite coronary artery involvement, which, it should be remembered, can exist without causing pain of any sort, then the rest must be absolute and prolonged Four weeks is the irreducible minimum During that time the patient must use the bed pan unless as not uncommonly happens, the strain is too great, then the sentence may be commuted to the commode The doctor must use judgment

Those in whose families cardiovascular disease has occurred should either not smoke at all or should use tobacco with great moderation

The meals should be small, especially the evening meal, and the food simply prepared. Unless there are complications, no special dietetic restrictions are necessary except that pastry, fried food, fresh bread, etc., should be omitted

One of the bugbears of myocardial patients is gas, which is usually attributed to some article of the diet I have however observed just as much distress, often even more, after a light meal such as a cup of broth, a glass of milk, or even a glass of water as after a mixed meal Fluids in excess cause discomfort—I limit my patients to 1200 cc, which includes water, milk, broths, orange and other fruit juices, all measured as liquids There are particular cases that may have to be put on a milk diet or upon butter milk or acidophilus milk for a few days in the beginning of treatment but after improvement, cereals, dry or cooked, with sugar rather than with salt, chicken, chops, oysters, cooked green vegetables, stewed fruit, especially apple sauce, orange juice, thin toast (Melba toast) may be added.

I am very partial to the use of sugar in some form in myocardial cases and sometimes prescribe pure cake chocolate—not milk chocolate

If patients complain of a bad taste or have a dry tongue I order the chewing of gum, an all too popular habit that I despise in health but encourage in sickness

If the gas is not controlled by diet, an enema will usually give relief Hot compresses, flaxseed poultices, the rectal tube, pituitrin are measures to combat the severer cases of distension

Insomnia is often the most distressing of all symptoms. Sometimes the bromids suffice although usually stronger remedies must be given—alonal, medinal, etc. But in the majority of cases nothing is so helpful as the opiates, preferably codein, but there should be no hesitation in giving morphin sulphate hypodermically in grains  $\frac{1}{8}$  to  $\frac{1}{4}$  with a little atropin. When morphin is used there is of course some danger of habituation but by gradually reducing the dose or occasionally substituting distilled water one can guard against this.

*Digitalis* In the severe coronary cases I prefer to wait with the use of digitalis until the hyperacute symptoms have abated. Then and in other myocardial cases from the beginning digitalis may be given in moderate doses. It will be found beneficial whether fibrillation exists or not. I shall not say much about the other cardiac stimulants except that my preference is for caffein sodiobenzoate.

*Psychotherapy* This is the most important part of the treatment. In no condition is the influence of mind over matter so clearly exhibited. An encouraging word or gesture makes the

patient eat and sleep better with all the good results that ensue therefrom.

*Nauheim Treatment.* I have seen good results from treatment at spas, especially Nauheim, and from similar treatment at home. It is unnecessary however to go into details.

*Exercise* In the severe cases, especially in those dependent upon coronary disease, exercise is forbidden for a long time. As Sir Clifford Allbutt has said, "The patient must crawl before he can walk." The passion for golf often drives men to over-exert themselves, to do more than the circulation can stand.

The first thing the patient does when he is better is to sit up in bed, then he sits in a chair for increasing periods, then he takes short level walks, then a motor ride of one hour from room back to room, then longer walks and rides, then lastly, a little golf on a non-hilly course.

By such measures many a man who has shown definite physical and electrocardiographic evidence of myocardial disease may be restored to health and usefulness. But if he has offended nature he must be told as a final injunction, "Go and sin no more."

# Undulant Fever in the United States\*

By GEORGE BLUMER, *New Haven, Connecticut*

IT is the purpose of this paper to discuss the following aspects of the problem of undulant fever in the continental United States (1) its incidence and distribution, (2) its origin and (3) the best methods for its detection

## THE INCIDENCE AND DISTRIBUTION OF UNDULANT FEVER

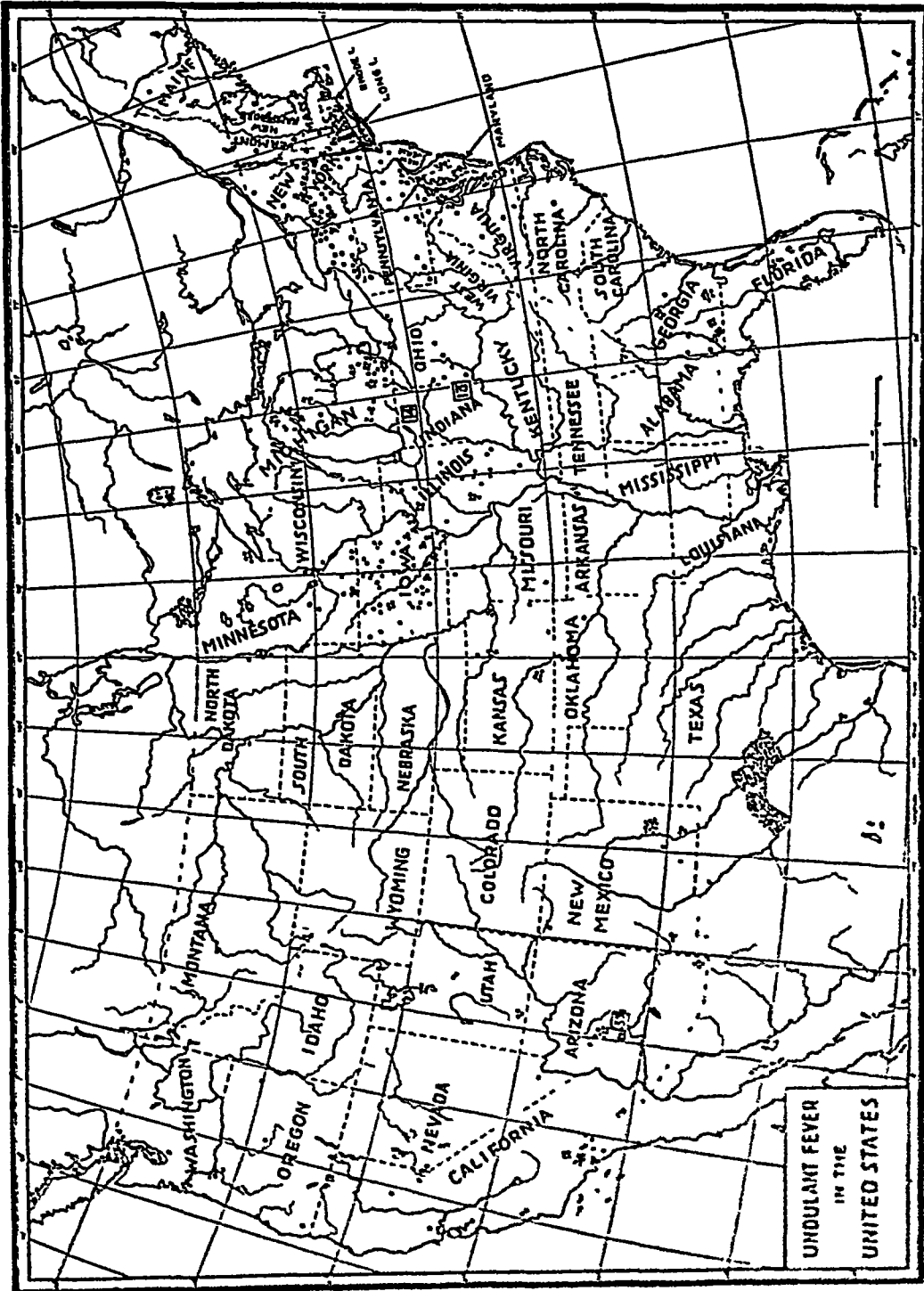
The incidence and distribution of undulant fever in the continental United States, so far as this can be discovered from the literature and by correspondence with state health departments, is shown by the accompanying spot map (Fig 1) Before discussing this map it must be explained, first, that no reports were received from the states of Oklahoma and Tennessee and second, that in the states of

Alabama, Arkansas, Colorado, Idaho, New Hampshire, Rhode Island, West Virginia and Wyoming no cases had been reported or come to the knowledge of the State Department of Health Inasmuch as the disease is not a reportable one in many of these states this must certainly not be regarded as evidence that the disease does not exist in them It can hardly be doubted that it occurs in every state in the union It should also be noted that in the map cases are credited, when that is possible, to their place of origin rather than to the place where a diagnosis was made It is not claimed that the map is absolutely accurate but it is at least approximately so and it is certainly accurate enough to serve as a basis for comment and discussion The map shows that up to date reports are available of 856 cases in the continental United States, distributed as noted in Table I

\*Read before the American College of Physicians, Boston, April , 1929

TABLE I  
*Undulant Fever Cases by States*

Arizona	69	Iowa	162	Mississippi	3	Ohio	20
California	29	Kansas	17	Missouri	31	Oregon	13
Connecticut	18	Kentucky	43	Montana	2	Pennsylvania	22
Delaware	3	Louisiana	1	Nevada	3	South Carolina	2
Dist of Columbia	5	Maine	9	New Jersey	3	South Dakota	2
Florida	1	Maryland	13	New Mexico	18	Texas	62
Georgia	37	Massachusetts	2	New York	76	Utah	8
Illinois	33	Michigan	73	North Carolina	3	Vermont	3
Indiana	32	Minnesota	20	North Dakota	4	Virginia	5
						Washington	3
						Wisconsin	6



Several things can be noted from a study of the map, of which the following are perhaps the most important

(1) That there are large areas in the country from which no cases have been reported

(2) That there is a permanent local focus of goat infection in Texas

(3) That the extent of infection in those states from which the disease is reported varies greatly

(4) That in heavily infected states such, for example, as Iowa or New York, the disease is widely disseminated and occurs both in the country districts and in large cities

(5) That, in addition to isolated cases, family outbreaks and institutional outbreaks, though uncommon, have occurred. The only real city outbreak was that at Phoenix, Arizona, in 1922, from infected goat's milk. It is permissible, we think, to speak of state-wide outbreaks in Iowa, New York and Michigan.

With regard to the states from which no cases have been reported, it is to be noted, as remarked above, that the disease is a non-reportable one in many of them. However, in other

states where the disease is also non-reportable cases have been detected and have been recorded in the literature. We can hardly assume, I think, that any one state or group of states has any monopoly of physicians who are unaware of the existence of the disease, and who overlook it. It is undoubtedly true that some health departments and some physicians are more keenly alive to the possible existence of the disease in their territory than others. In some states the routine testing of sera sent in for the Widal or Wassermann tests has led to the detection of unsuspected cases and has stimulated interest in the disease.

The disease as originally described, i.e. as a goat-transmitted infection, has existed in Texas for at least forty years. In their 1911 report Gentry and Ferenbaugh state that it had then been known in Edwards County for twenty-five years. Foci connected with the goat raising industry have also been known for many years in certain parts of Arizona and New Mexico and it is to be expected that undulant fever of caprine origin will be found wherever goat raising is a prominent industry. (See Table 2)

TABLE 2  
*Number of Goats in States having over 1,000*

Texas	1,791,325	Utah	48,292	Nebraska	2,952
Arizona	281,564	Florida	36,944	Wisconsin	2,893
New Mexico	240,067	Kentucky	33,255	New York	2,542
Oregon	21,193	Oklahoma	32,436	Minnesota	2,082
Missouri	118,316	Colorado	21,525	Ohio	2,001
California	98,859	South Carolina	16,395	Idaho	1,602
Arkansas	95,731	North Carolina	15,959	Pennsylvania	1,536
Georgia	90,606	Virginia	5,774	Montana	1,475
Alabama	72,469	Washington	5,586	South Dakota	1,396
Mississippi	64,947	Kansas	5,581	Wyoming	1,152
Tennessee	63,154	Iowa	5,435	North Dakota	1,064
Louisiana	59,767	Indiana	3,995	Michigan	1,015
		West Virginia	3,994		

The variable extent of the disease in different states will probably not be satisfactorily explained until we have more exact knowledge of its origin and the method or methods of its transmission. It is clear that in most infected states it is entirely independent of the goat-raising industry and we may at once discuss as satisfactorily proven the caprine origin of certain groups of cases and concentrate our attention on those cases which are not due to goat's milk or its products. It is proper also to place in the category of proven cases those occupational ones of porcine origin which occur among slaughter-house employees and laboratory infections in bacteriologists. From an epidemiological viewpoint it is the cases which are now quite generally assumed to be due to cow's milk infected with the *B. abortus* type of organism which should claim our attention.

#### THE ORIGIN OF UNDULANT FEVER IN THE UNITED STATES

We have already stated that there are two groups of cases concerning the origin of which no doubt exists (1) the group associated with the goat-raising industry, (2) the occupational groups of porcine or laboratory origin. It has been quite generally assumed by health authorities that cases not of caprine or porcine origin are due to the transmission through cow's milk of the *abortus* type of *Brucella* originally described by Bang of Copenhagen and referred to in the older literature as the *Bacillus abortus* of Bang. Anyone who has read the literature carefully must have been struck by the fact that decisive proof that the milk of cattle

suffering from contagious abortion can transmit undulant fever to man is lacking in many instances. We shall attempt to state and evaluate some of the known facts for and against the transmission of undulant fever by infected cow's milk.

1 It is known that contagious abortion among cattle is a disease which is widespread throughout many parts of this country. (See Table 3.) Exact information as to its prevalence in some states is lacking but there is enough evidence to clearly demonstrate that, allowing for the sterilizing effect of pasteurization, a considerable proportion of the market milk of many states is contaminated with living *Brucella abortus* of the bovine type.

2 It is known that undulant fever is least common among those members of the community who drink the largest amount of milk, namely, children. In Denmark, where an analogous situation exists, Madsen states: "No case has ever been observed in the hospitals and the asylums for children in Copenhagen or elsewhere where milk is used in large quantities."

3 The actual experiments of feeding healthy individuals with milk known to be infected with *Brucella abortus* has been made with negative results. In the experiment of Coolidge a feeding of the milk with six people some of whom contracted undulant fever. In connection with this observation it is pointed out that the cause of the infection was human beings and not *Brucella abortus* that served as the source of the infection. The cause of the infection of the milk was not *Brucella abortus*.

TABLE 3  
*Occurrence of Infectious Abortion Among Dairy Herds*

California	Some herds heavily infected
Connecticut	About 90% of herds infected
Florida	A considerable amount of infection
Georgia	Infection of herds quite common
Indiana	50% of herds infected
Iowa	Infected herds common
Maine	60-80% of herds infected
Massachusetts	Widespread heavy infection of herds
Minnesota	Infection of dairy herds present
Michigan	Infection prevalent
New Hampshire	Large incidence of infection
New York	Estimated that 30% of herds are infected
Ohio	Widespread infection of dairy herds
Oregon	Infection widespread
Pennsylvania	Infection of herds fairly prevalent
Vermont	75% of herds infected
Washington	25 to 5% of herds infected

Against these negative observations one must place certain apparently positive ones. For example, the report made by Dr. G. E. Atwood, Health Officer of Waycross, Georgia, of six cases of undulant fever in one family all supplied by the milk of one cow which died of some unknown disease before its blood or milk could be tested. Even where the chain of circumstances is seemingly as obvious as this, however, it must be remembered that the mere fact that infection through cow's milk is generally regarded as probable may have led to the overlooking of some other source of infection.

The real difficulty in deciding the type of infecting organism is a bacteriological one. It is often a simple matter to prove that an individual is infected with an organism of the *Brucella* group, but it is much more difficult to decide which particular member of the group is responsible. There is no question as to the pathogenicity of the caprine type (*Brucella*

*melitensis*\*) The difficulty lies in distinguishing the bovine from the porcine type. As Blake and Oard have pointed out there are three methods of doing this: (1) the guinea pig inoculation test (Theobald Smith), (2) the agglutinin absorption test (Alice Evans), and (3) the bacterial metabolic tests (McAlpine and Slanetz). It is noteworthy that but few organisms isolated from human cases have been submitted to all three tests. Such evidence as exists at the present time regarding the pathogenicity for man of the bovine and porcine types of *Brucella abortus* suggests very strongly that it is the porcine type which is responsible, even in those cases which appear to be transmitted by cow's milk. In a recent letter Theobald Smith

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\*The bacteriological nomenclature of the group is in a state of confusion because different bacteriologists have adopted different classifications. In this paper *Brucella melitensis* refers to the caprine type. The other two types are referred to as *Brucella abortus* (bovine) and *Brucella abortus* (porcine).

says "I may say that thus far none of the twenty-five or more cultures from human beings in this country which I have studied are precisely like the bovine type" To this evidence we may add that of McAlpine and Slanetz, who state that all organisms of human origin which they have studied have proven to be of the porcine type

unwise in the present state of our knowledge to draw the definite conclusion that most of the recent cases of undulant fever are due to *Brucella abortus* of the porcine type

There are other factors which must certainly be taken into consideration There is always the possibility that *Brucella abortus* of the bovine type

TABLE 4\*  
*States in which there are over 1,000,000 Hogs, 1928*

Iowa	10,650,000	Indiana	2,227,000	Texas	1,375,000
Illinois	5,039,000	South Dakota	2,445,000	Oklahoma	1,104,000
Missouri	4,720,000	Kansas	2,320,000	Arkansas	1,088,000
Ohio	2,537,000	Wisconsin	1,863,000	Tennessee	1,084,000
Minnesota	3,710,000	Georgia	1,424,000	Kentucky	1,081,000

\*Year Book of Agriculture, 1927

We are forced to conclude that up to the present, at least, there has not been sufficient study of the origin of undulant fever, which is not of caprine or occupational origin, to enable us to reach a definite decision as to the source of the infecting organism The small amount of accurate evidence now in existence definitely points towards the porcine type of *Brucella abortus* rather than the bovine type This does not eliminate cow's milk as a source of infection for the reason that cattle as well as man may be infected by the porcine type of *Brucella abortus* The obvious suggestion which this fact carries is that where undulant fever is transmitted to man through infected cow's milk the cattle have been infected with the porcine type of organism rather than with the ordinary bovine type It is perhaps significant that the largest number of reported cases have come from the state of Iowa, which is notoriously a hog-raising state However, it would be

may, in certain localities, have taken on increased pathogenicity, a phenomenon often observed in connection with epidemics of bacterial disease, though not yet satisfactorily explained The decided increase in recent years of infectious abortion in cattle, pointed out by Mohler, suggests this possibility Indeed, in view of the rapid increase in the number of human cases reported within the past three years we are justified in suspecting that such a phenomenon is now taking place It is questionable whether this comparatively sudden increase in the number of reported cases of undulant fever can be explained solely on the ground that the profession and health departments have become more acutely aware of the disease

#### CLINICAL DICTION OF UNDULANT FEVER

As one of our surgical colleagues recently remarked "the key which opens the door of diagnosis is suspi-



cion" Practitioners have always met with obscure fevers. In the older books these are often described under the vague heading of febricula. As new febrile diseases are discovered the number of cases of obscure fever should diminish. We should be suspicious that any unexplained fever, especially if it assumes an undulant type, is undulant fever. Even in the case of single attacks of fever of comparatively brief duration we should think of undulant fever because there is a mild, often ambulatory, type of the disease in which only a single bout of fever occurs.

A point which has struck the writer in the limited number of cases he has seen is the singular lack of discomfort which some of these patients exhibit. They appear to be able to attend to their ordinary work, at any rate in the earlier weeks of the disease, when they are carrying a fever which would ordinarily interfere with such duties. Furthermore, particularly in the early stages, there is a singular lack of physical signs in many of the patients. In the prolonged cases this ceases to be true in the later stages.

The most satisfactory method of diagnosis is the recovery of some type of *Brucella* from the circulating blood. The blood should be taken during a febrile period and preferably at the height of a paroxysm. The culture should be observed for a long period. The ordinary routine of many bacteriological laboratories whereby cultures are discarded as negative after three or four days will certainly result in the overlooking of some cases. In view of what has been said in the preceding discussion it is important

that where organisms are isolated they should be submitted to a skilled bacteriologist and an attempt should be made to determine the exact strain of the *Brucella* which is present. At times the organism can be isolated from the urine without difficulty, so that urinary cultures are always worth while in doubtful fever cases.

Lacking blood cultures the agglutination test done under proper precautions is of great value. In childhood the blood of a small proportion of individuals contains agglutinins which act in titres as high as 1:300. Several serologists state also that the blood serum of adults may cause agglutination in titres as high as 1:160, even when there is no history remotely suggesting undulant fever. It is thought that these reactions may possibly occur as a result of the ingestion of *Brucella abortus* in cow's milk. Evans suggests that the reaction is a specific response, while other writers think that the phenomenon is one of passive immunity. Whatever the explanation may be these observations make it clear that agglutination by serum in low dilution cannot be regarded as proof of the presence of undulant fever. The titre of agglutination must be a high one before it is regarded as satisfactory evidence of the presence of the disease.

#### CONCLUSION

It is apparent that there has been an increasingly large number of cases of undulant fever reported in the United States during the past two or three years and it cannot be positively asserted that this increase is entirely due to an awakening on the part of health authorities and physicians to the fact that this disease is to be considered in

the diagnosis of obscure fevers. This increase in reported cases of undulant fever has not occurred in the group of cases which are connected with the goat industry. Two small groups of occupational cases of porcine or human origin occurring in slaughterhouse employees and laboratory workers have been split off from the main group, but the great majority of cases recently reported have occurred in individuals who were not obviously in contact with either goats or hogs. The bacteriological evidence as to the origin of these cases is incomplete but definitely points to a porcine rather than a bovine origin, and inasmuch as cattle

are susceptible to infection with the porcine type of *Brucella abortus* the evidence suggests the possibility that cow's milk can, under certain circumstances, transmit the disease. There is need for more careful bacteriological and epidemiological study of the disease. If, as now seems possible, the disease is really on the increase, it will be necessary, in order to control it, to obtain accurate knowledge as to its method of spread. It is also important to determine this, lest, in their enthusiasm, state legislatures begin to pass unwise laws relating to infected cattle and to the distribution or handling of milk and milk products.

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# Pernicious Anemia as a Deficiency Disease\*

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**I**N discussing the nature of Pernicious Anemia, we wish to confine ourselves strictly to the idiopathic anemia described by Addison and later by Biermer, and differentiate it as sharply as possible from other anemias with similar blood pictures

In Addisonian Anemia three organ systems are dominantly affected, the gastro-intestinal tract, the blood, and the central nervous system

The lesions in the gastrointestinal tract are glossitis, and an achylia gastrica associated with an atrophy of the gastric mucosa. Both pepsin and HCl are lacking in the gastric secretions, and injections of histamine do not lead to any secretion of acid as is the case in functional achylia. Levine and Ladd,<sup>1</sup> in analyzing 122 cases of Addison's anemia, have found but one case that failed to show achylia, and other workers have found this association so constant that it is now felt that achylia is a necessary finding in making the diagnosis of Pernicious Anemia. More interesting still are reports by Levine and Ladd, Hurst,<sup>2</sup> Wilkinson<sup>3</sup> and others that achylia had existed, 10, 13 and even 20 years before the anemia developed. In this connection Hartman<sup>4</sup> and Sir Barclay Moynihan<sup>5</sup> have re-

ported the development of a pernicious anemia blood picture following total gastrectomy. Finally, all reports to date agree that with the liver diet, while the blood improves dramatically and the cord symptoms improve somewhat or are arrested, the achylia persists unaltered. The achylia then, is invariably associated with the disease, antedates it in time, and persists after the return of the blood picture to normal.

The blood picture consisting of a marked reduction in red cells, high color index, megalocytosis, poikilocytosis, leukopenia and reduction of platelets is well known, while the high serum bilirubin, the increased excretion of urobilin in stools and urine, and the marked deposits of hemosiderin in the liver, spleen and kidneys are the classic arguments in favor of a hemolytic anemia. The blood cholesterol is also reduced,<sup>6</sup> and the red cells slightly less fragile than normal.

Of greater interest than the peripheral blood are the findings in the bone marrow. The constant autopsy finding of replacement of the fatty marrow of the long bones with red marrow very rich in megaloblasts has been extended by the observations of Peabody.<sup>7</sup> By trephining the tibia he was able to observe the marrow from the most

\*Read before the American College of Physicians, Boston, April 8, 1929

severe stages of the disease through to remission. As the condition of the patient and the peripheral blood picture improved the marrow picture changed from the megaloblastic hyperplastic marrow to the normal adult fatty marrow. Megaloblastic hypertrophic marrow coincided with relapse, normal marrow with remission, and these changes follow the institution of liver diet or potent liver extracts. The outpouring of reticulocytes which had been observed in the pre-liver era before spontaneous remissions, has been shown by Minot<sup>6</sup> and his colleagues to occur regularly about a week after beginning the liver diet, and the feeding of liver in some way enables a hyperplastic marrow filled with megaloblasts to convert these immature red cells into mature forms which enter the peripheral circulation. Whether this is done by neutralizing an hypothetical toxin or supplying missing building blocks will be considered shortly. Coincident with the blood and marrow improvement just mentioned, serum bilirubin, urobilin in stool and urine, and blood cholesterol return to normal. It is also interesting that in those cases having edema, a diuresis occurs shortly after the liver diet is started.

The changes in the central nervous system may occur with the anemia or alone, they are always, however, associated with achylia. The essential lesion, according to Collier,<sup>7</sup> is a primary degeneration of the myelin sheath, with no glia reaction. The tracts most often affected are the dorsal columns and the pyramidal tracts with the usual symptoms of loss of function of these pathways. There

are in addition scattered patches of degeneration of the white matter throughout the cord and brain itself. In the great majority of cases the cord lesions are usually arrested, and in some instances markedly improved by the liver diet.

Such in brief are the pathological changes encountered in Addison's anemia, and their response to liver therapy. One other point may bear on the nature of the disease, its racial distribution. It is largely a disease of the so-called Nordic races, and is most prevalent in the Scandinavian countries, Great Britain, Germany, Canada and the United States. It is almost unknown in China, South America and Java. Draper<sup>10</sup> has found that on measuring pernicious anemia patients anthropologically that these measurements correspond closely to "eunuchoid" type, and that the pernicious anemia group have more nearly similar anthropological measurements than any other disease group that he has studied. This points toward a constitutional factor in this disease, and it is not impossible that the omnipresent achylia may be on a constitutional basis.

The nature of the active substance in liver also throws some light on the nature of the disease. The Lilly Extract, which produces all the effects on the blood that have been noted for whole liver, as prepared by Cohn's method<sup>11</sup> is essentially a watery extract of liver, with the proteins removed by heating to 80° in acid solution. The active material is then carried down with the precipitate on pouring into very concentrated alcoholic solution. Further chemical studies carried

out at Harvard and Columbia<sup>12</sup> have agreed in essential points. The active material is not precipitated by sodium sulphate nor basic lead acetate, but is precipitated by phosphotungstic acid and can be regenerated with baryta. From this point on evidence has been obtained that the material is not precipitated by alkaline silver solutions, and that by appropriately fractioning with acetone a biuret negative material can be obtained which is active. We appear to be dealing with an organic base, not precipitable by silver, at least in impure solutions. Of the pure substances that might have been in the best fractions the following have been fed to patients with negative results: spermine, ergothioneine, choline, histamine, histidine.

The best fractions have been effective in doses of about a gram daily, and once half a gram gave a good response. P has been absent, and N about 12%. Fe is absent.

McCann<sup>13</sup> has fed liver ash in 4 gm doses daily with negative results.

We have then a mixture of organic bases effective in the doses mentioned.

Most important experiments as to the nature of the disease are those of Castle<sup>14</sup> of Boston. He has found that cases of pernicious anemia did not improve on a diet containing a half pound of lean meat (muscle) daily, but that when the meat was first eaten by a normal individual, regurgitated after 30 minutes, then incubated with HCl for two hours and fed by stomach tube daily, the response of reticulocytes and the rest of the blood picture was similar to that obtained with liver. This is very strong evidence in favor of the view that the gastric di-

gestion of muscle liberates a substance which exists free in liver and kidney, and which is an essential building block for red cells.

For many years upper intestinal sepsis secondary to achylia has been held responsible for the hypothetical toxin of Addison's anemia. Recently Morton, Kahn, and Torry,<sup>15</sup> have produced an anemia in rabbits by injecting the marrow cavity with B. Welchii toxin. The blood picture has resembled that of pernicious anemia and was improved by liver extract. Several years ago we gave a man suffering with pernicious anemia 200 of B. Welchii antitoxin, and his serum contained circulating antitoxin for two weeks, protecting mice from death and red cells from hemolysis with known B. Welchii toxin. There was, however, no improvement in his blood picture nor general condition.

Ashford<sup>16</sup> and others have reported improvement in the anemia of tropical sprue on liver extract. We too have observed the reticulocyte response with a liver fraction in a case of sprue anemia with adequate gastric HCl, and most interestingly Ashford has noted a reticulocyte response from 1 to 10% with RBC at 1 million on a meat diet in a sprue patient with HCl in the stomach. It seems possible that the pancreatic digestive disturbance in sprue may in some way function analogously to the gastric fault in pernicious anemia as etiologic factor in the anemia.

Response of Bothriocephalus anemia to the liver diet is cited by Syderhelm<sup>17</sup> as evidence that the liver diet works by neutralizing a hypothetical toxin. The explanation of the results in this

anemia can only be answered by further investigation

We have observed two cases of Laennec's cirrhosis of the liver with a secondary anemia of 15 million red cells each of whom had a reticulocyte rise from 2 to 12% on liver extract. The explanation is obscure. There was acid in the stomach of one, the other had no gastric analysis.

Peabody concluded, after his bone marrow studies that "the course of the anemia" appeared to be "an abnormal type of cell growth consisting in the development of the primitive myeloblast and a failure of differentiation into more mature cells that normally go into the blood."

Minot has shown that the feeding of liver is followed by the appearance of reticulocytes and then mature cells in the blood. Cohn has shown that a gram or so of organic bases from liver a day will accomplish this, and Castle that lean meat, itself ineffective, will accomplish the same result after digestion in a normal stomach. This evidence places the burden of proof on

those denying the hypothesis that pernicious anemia is a unique deficiency disease, secondary to a fault in gastric digestion, and that the active substance which is necessary for the maturation of the megaloblast, while free in liver, exists in a combined form in muscle, and probably many other sources. The high urobilin excretion, and organ hemosiderin, are better interpreted as excess of hemoglobin building material which cannot be utilized by an imperfectly functioning bone marrow, than as an evidence of blood destruction. Other anemias known to be due to blood destruction are accompanied by reticulocytosis, pernicious anemia is not until a gram or so of hepatic bases are supplied daily.

It seems, therefore, that there is a substance free in liver, and freed by gastric digestion in meats and probably other foodstuffs, which is necessary for the formation of adult red blood cells, and that the lack of this substance due to faulty gastric digestion gives rise to the picture of pernicious anemia.

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# The Significance of Glycosuria\*†

By JAMES E. PAULLIN, M.D., *Atlanta, Georgia*

WHEN a reducing substance is found in the urine during the course of a routine physical examination, or a patient states that such a substance has previously been found, two questions immediately present themselves for solution (1) Is the reducing substance glucose? (2) If it is glucose, what condition is responsible for its presence? Upon a correct solution of these problems depends the future welfare and comfort of the patient. It is the purpose of this paper to discuss briefly some of the procedures which are useful in answering these questions.

For several years there has been quite a discussion as to whether human urine normally contains glucose. The statement of Baish<sup>1</sup> in 1895 that normal human urine contained a carbohydrate, probably dextrose, has received the support of Benedict, Osterberg and Neuwirth;<sup>2</sup> these writers believe that there is normally present in urine a detectable and measurable quantity of glucose which does not reduce the copper solutions generally employed. This substance can be increased by feeding carbohydrate, and to this condition they have given the name "glycuresis." Additional evidence

is furnished by Blatherwick, Bell, Hill and Long,<sup>3</sup> Malmros<sup>4</sup> says "Even though it has not been possible to produce a chemical analytically perfectly valid proof, the investigations still indicate that glucose occurs in normal urine." On the other hand Folin and Berglund<sup>5</sup> believe that the carbohydrate occurring in normal urine is not glucose, but a substance derived from nuts, fruits, grains and the decomposition products of foods caused by cooking. Greenwald, Gross and Samet,<sup>6</sup> Shaffer and Hartman,<sup>7</sup> Eagle,<sup>8</sup> and others are of the opinion that the reducing substance is not glucose, and as such, does not occur in normal human urine. As yet the controversy cannot be said to have been definitely settled, the weight of evidence seems to be that glucose, per se, does not occur in normal urine. The carbohydrate under discussion, whatever it is, does not interfere with the determination of glucose, present in pathological amounts, which is easily detectable because it produces certain definite changes in the color and transparency of the various copper solutions in general use.

It is common knowledge that other sugars and substances than glucose will give positive reduction tests. Among these are lactose, maltose, pentose, and levulose. These can be dif-

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ferentiated from glucose by employing the fermentation test, phenylhydrazin test, the use of the polariscope, and other chemical reactions, viz, Rubner's test and mucic acid test, in differentiating lactose, the Bial test for differentiating pentose, and Seliwanoff's test for differentiating levulose. There is a sufficient difference in the reactions of the various sugars to these procedures to make their differentiation possible. Such substances as uric acid and creatinin occurring in concentrated urines will at times produce a typical reduction of the various copper solutions. These can be easily differentiated by diluting the urine and further testing. Chloroform when used as a preservative may give a positive reduction test. The conjugated glycuronates which occur after the administration of certain drugs—chloral, turpentine, camphor, menthol and phenol—may be confused with glucose. The reduction produced by these substances is not the typical reaction observed when glucose is present. The glycuronates do not ferment with yeast and do not form osazone crystals with phenylhydrazin. Glucose produces a typical reduction with Benedict's solution or Nylander's reagent, it readily ferments with yeast, is dextrorotary and forms characteristic osazone crystals with phenylhydrazin.

Having determined that the reducing substance is glucose one may ask: What is the nature of the disturbance causing its presence? Is the fault primarily renal or is it a manifestation of some metabolic disorder? To determine this we have several procedures which are of value in clarifying the situation. 1. Testing each speci-

men of urine voided during the twenty-four hours to determine whether sugar is constantly or intermittently excreted.

2. Determining the blood sugar level after a night's fast and again two hours after the ingestion of a meal containing an ordinary helping of sugar, bread, potatoes, and dessert.

3. Utilization of the glucose tolerance test which consists of simultaneous observation at frequent intervals of the blood sugar level and urinary sugar content, following the ingestion of a definite amount of glucose dissolved in water. Before using this test it is of importance to know that the patient has not been, for any length of time, on a restricted carbohydrate diet. It has been demonstrated many times that a normal individual subsisting on a diet low in carbohydrate, when subjected to a sugar tolerance test, will respond with a marked and prolonged hyperglycemia and glycosuria which would not occur had the previous diet contained the average carbohydrate ordinarily consumed. According to the results obtained from these observations it will be possible to classify the individual as belonging to one of the following groups.

I. Renal Glycosuria. This condition is characterized by the constant presence of glucose in the urine. The sugar is excreted with a blood sugar level which is normal or subnormal. The renal threshold is low and it is supposed that the kidney is unable to prevent the excretion of sugar, which is probably a congenital or hereditary anomaly. Patients with this condition store, utilize and metabolize glucose in a perfectly normal manner, the blood sugar response to the administration

of glucose does not exceed the normal level, the patient is free from all symptoms of diabetes mellitus and when observed over a long period of time does not develop this disease

constant presence of sugar in detectable and measurable amounts in the urine

II Cyclic Renal Glycosuria, Alimentary Glycosuria, or Alimentary

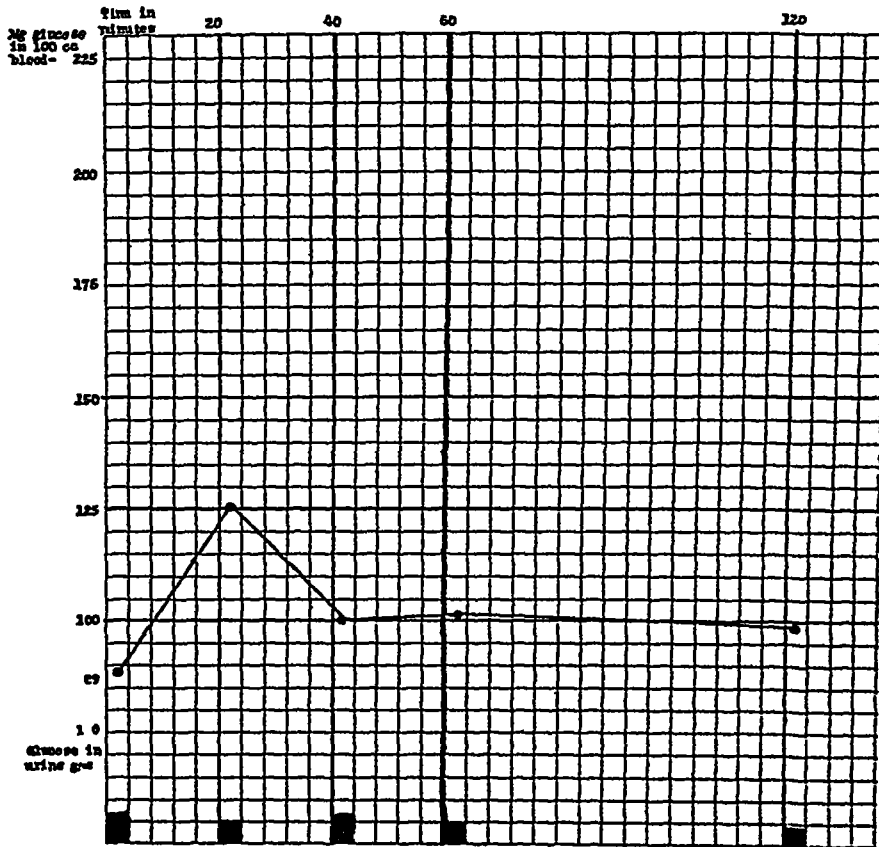


CHART I

Chart I graphically represents the behavior of the blood sugar and urinary sugar after the administration of 100 grams of glucose to a patient with renal diabetes. It is observed from this chart that the fasting blood sugar is at a normal or slightly subnormal level. Twenty minutes after the ingestion of 100 grams of glucose the blood sugar reaches its maximum level of 125. There is then a rapid decline within forty minutes to a level of 100 or it fluctuates slightly. There is a

Hyperglycemia. By these terms one understands that an otherwise normal, healthy individual excretes urinary sugar in detectable and measurable amounts after taking foods rich in sugar or starch. The glycosuria may be due to an abnormal post-prandial hyperglycemia or to a low renal threshold. Sugar is found in the urine from one to three hours after a meal. The fasting blood sugar is normal. The majority of these patients have a hyperglycemia following a meal.

taining the average amount of carbohydrate. As to whether these individuals are perfectly healthy is not definitely settled. Some evidence is at hand which would lead us to suppose that the alimentary hyperglycemia is probably due to insufficient insulin production, in this respect, resembling a true diabetic. After the administration of 100 gm of glucose the blood sugar reaches its peak within forty minutes to one hour and returns to a normal or subnormal level within three hours. As the sugar concentration in the blood rises glucose appears in the urine and continues to appear until concentration in the blood returns to a lower level than that at which it was first observed. Three or four hours after a sugar tol-

erance test an occasional person will exhibit evidence of hypoglycemic shock. This is supposedly due to an overproduction of insulin stimulated by the hyperglycemia, the pancreas getting a late start, but when once sufficiently stimulated continues with its supply to excess. A large series of these patients have recently been investigated by Malmros,<sup>4</sup> who believes that they have a benign glycosuria.

Chart II represents graphically the blood sugar and urinary sugar response of such a patient to the ingestion of 100 grams of glucose. It will be observed that following the administration of glucose the blood sugar rises from the normal level within forty minutes to the upper limit of normal

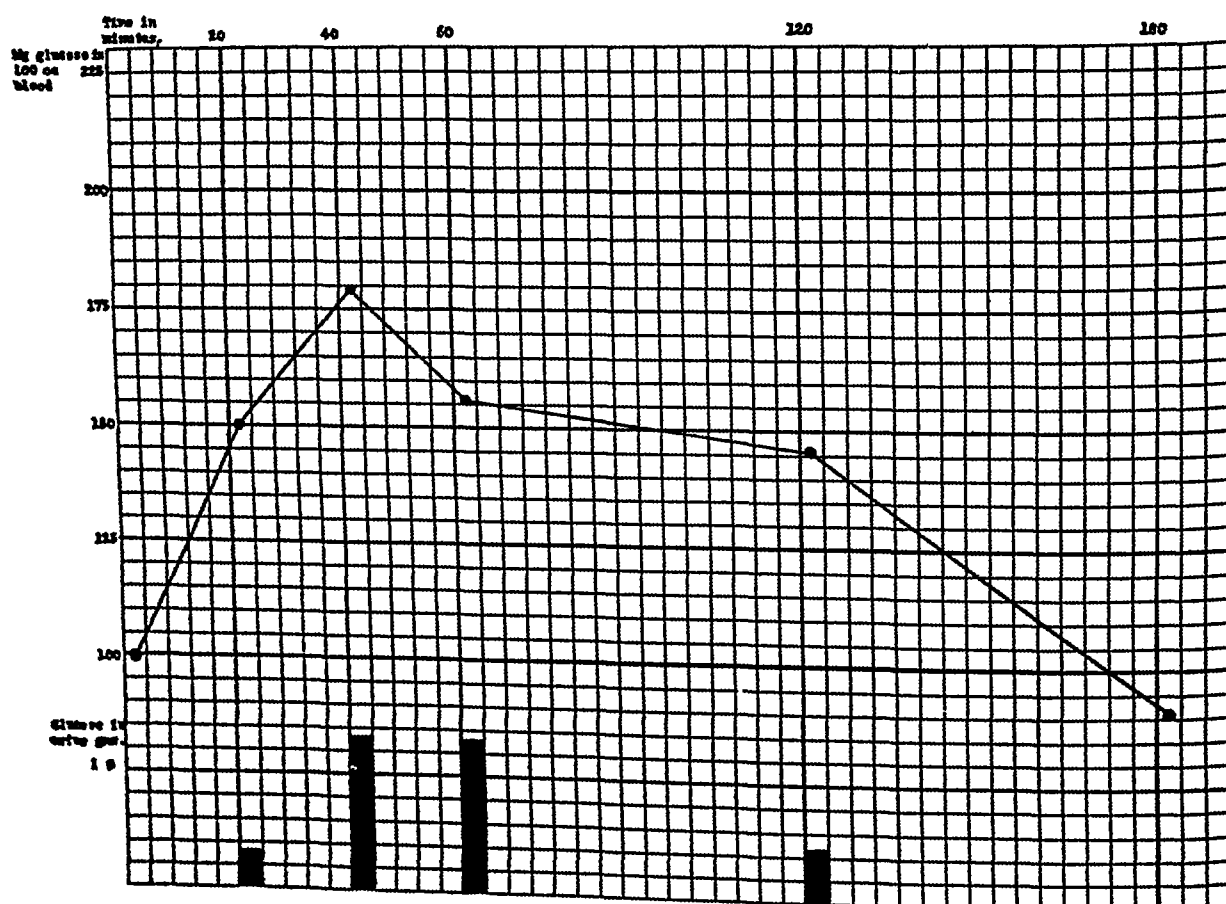


CHART II

and at the end of three hours is lower than at the beginning of the test. Sugar begins to make its appearance on the ascending side of the scale and is present in the urine with a blood sugar of 150, showing that the renal threshold in this particular patient is somewhat depressed. Sugar is present in the urine until the blood sugar level falls below 150 and at the end of three hours no sugar is observed.

III Diabetes Innocens. This name has been given to an unusual clinical condition which shows certain characteristics of diabetes mellitus and renal glycosuria. It apparently runs a harmless course. In patients with this condition the fasting blood sugar level is normal or subnormal. There is a

post-prandial hyperglycemia. The renal threshold is low, resembling that observed in renal glycosuria. Sugar is constantly excreted in the urine and there is an increase in glycosuria with an increased carbohydrate intake, but the increase is not commensurate with the increase in food. There are no symptoms of diabetes and a few patients observed over a period of years have so far not developed a symptomatic diabetes mellitus. There is no disturbance in the ability of the patient to metabolize, store and utilize glucose (Parsons) <sup>9</sup>. After a glucose tolerance test the blood sugar rises from the normal fasting level, within an hour, to a height resembling that observed in a diabetic. The normal fasting level

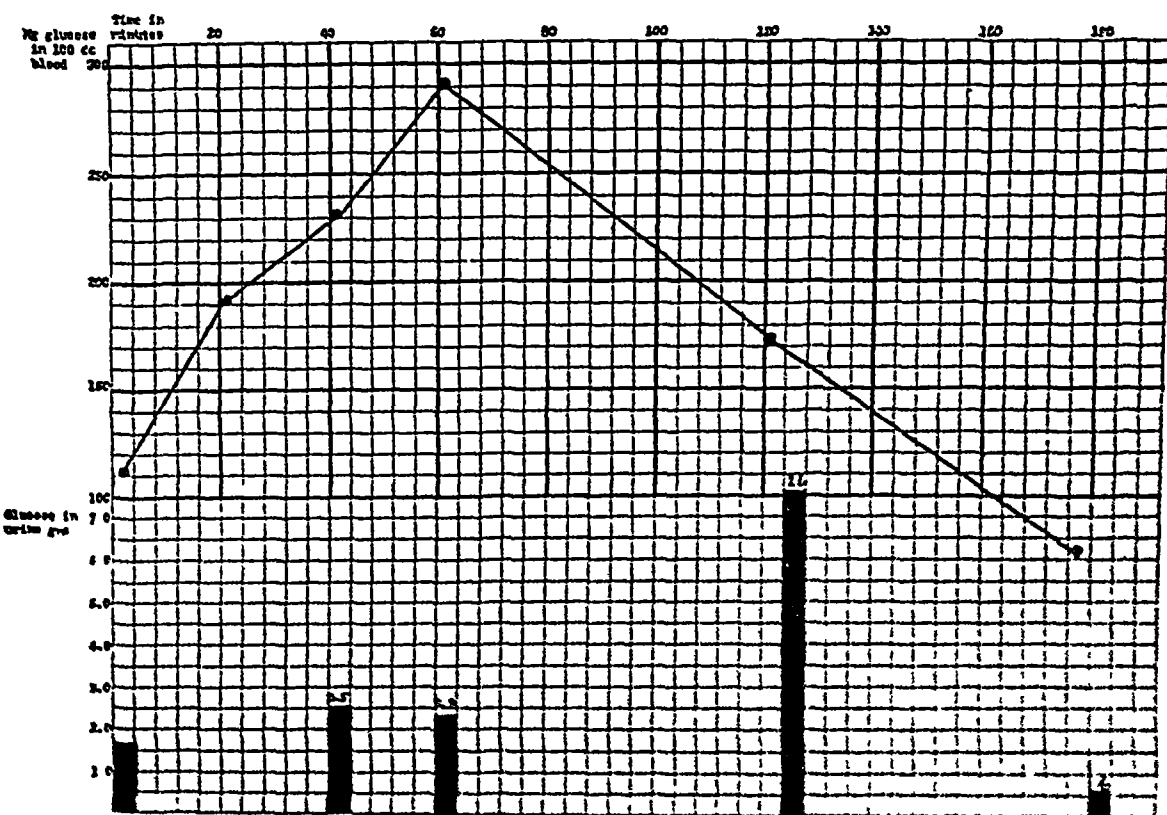


CHART III

is not reached until three hours after the administration of glucose. Sugar is constantly excreted in the urine.

Chart III graphically records the events in a patient with diabetes innocens following the administration of 100 grams of dextrose. It is observed that after one hour the blood sugar has reached a level of 290 mgms, at the end of two hours it is 175 mgms, at the end of three hours it is 75 mgms. During this entire time sugar is excreted in the urine in considerable amounts.

IV Diabetes Mellitus. In this disease the patient is unable to mobilize, utilize or metabolize glucose in a normal manner. Experimental and clinical

evidence leads us to believe that the causative factor is either a deficient insulin production or the production of an inferior quality. In the untreated cases the fasting blood sugar is above normal, rarely will one find a mild diabetic with a normal blood sugar. Glucose, as a rule, is constantly present in the urine and is greatest two or three hours after a meal containing carbohydrates, coincident with the glycosuria there is hyperglycemia. The renal threshold is normal or elevated. Because of the inability to properly metabolize glucose acidosis frequently develops.

This chart represents graphically the series of events occurring in a mild

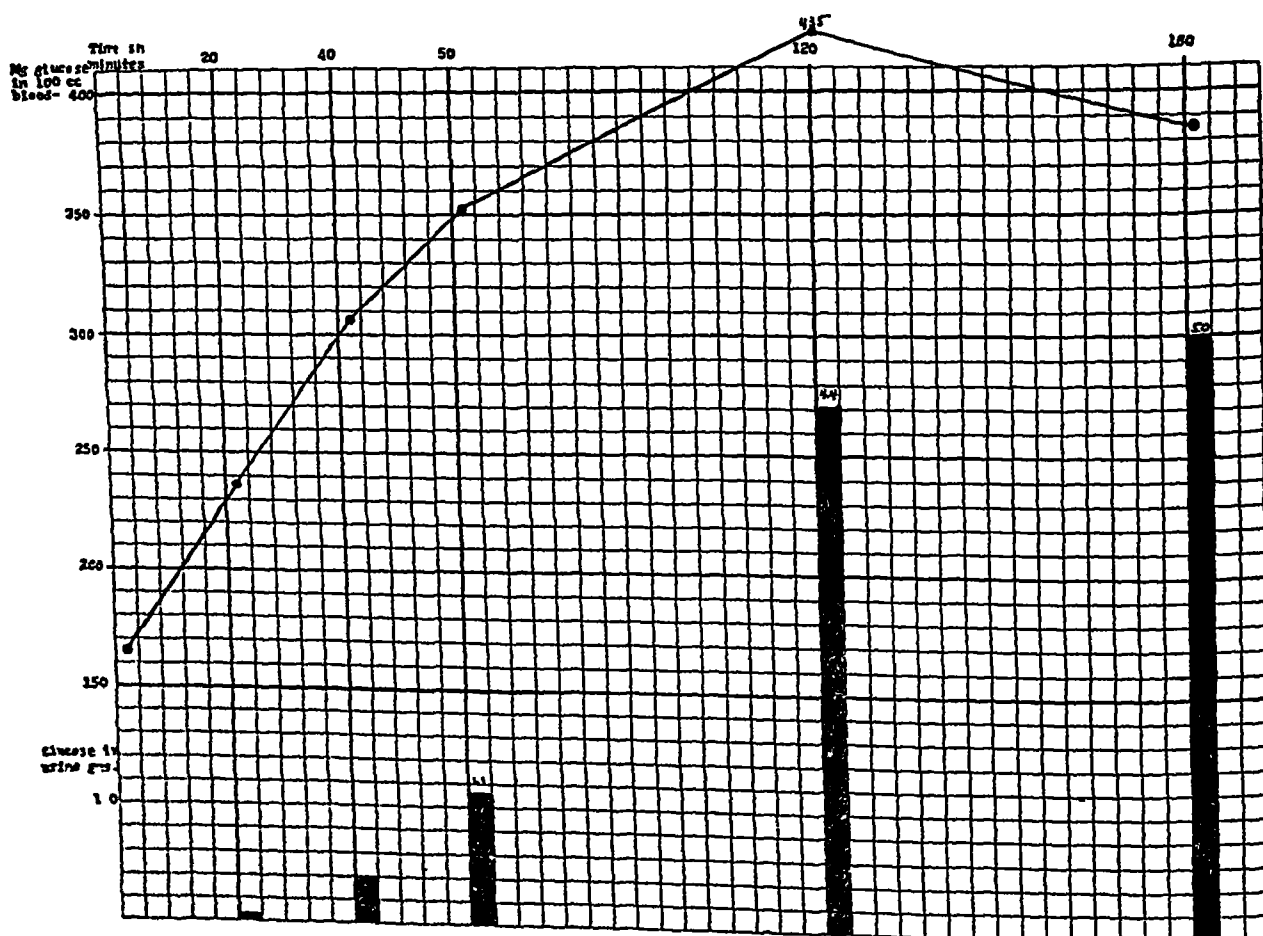


CHART IV

diabetic who was given 50 grams of glucose. It is observed that the fasting blood sugar is increased but there is no sugar in the urine voided at this time. The renal threshold is normal, or slightly increased, in this patient. The blood sugar at the end of two hours is 435 mgms per 100 cc. At the

end of three hours it is 385 mgms. There is a constant, steady increase in the amount of sugar voided in the urine.

Having determined, by using the methods outlined, to which group the individual belongs, appropriate treatment can be instituted.

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# A Surgeon's Views of the Treatment of Peptic Ulcer\*

By DAVID CHEEVER, M D , *Boston, Massachusetts*

NO man and no method have any monopoly of the successful treatment of peptic ulcer and in proof of this I am going to show this patient, Bennie Wean, who must be regarded as illustrating the unsuccessful treatment of ulcer by both medical and surgical means. The patient first came under observation on December 6, 1927. He is a Russian Jew, an upholsterer by trade, thirty years of age, and is married and has two children living and well. His family and previous history are both negative except for two attacks of tonsillitis fifteen years ago. His habits are good—he drinks not at all and smokes but little. He is constantly worried about his inability to earn a good living on account of his illness. This began about five years ago with a gnawing epigastric pain occurring an hour or two after eating and lasting but a few minutes. Later this became more constant and he discovered himself that it was relieved by taking food and also by taking soda which was advised by friends. After a year of varying degrees of misery he consulted a physician and was sent to an excellent hospital in Chicago (where he then lived) where he remained for

seven weeks under appropriate treatment for peptic ulcer. He was discharged relieved on a modified ulcer diet of milk, cream and farinaceous food, gradually returning to more normal diet. He followed this program with considerable faithfulness but found that on every relaxation his symptoms would recur. He never vomited or noticed blood in the stools. About December 1, 1927, the symptoms had become so much worse that he applied to the Brigham Hospital for help. Physical examination showed no deviation from the normal except for a point of moderate tenderness in the right upper quadrant close to the costal margin. Both tonsils and teeth were in excellent condition. The blood and urine were perfectly normal. Stools showed a benzidine reaction for blood. Gastric analysis showed no stasis, but hyperacidity, the free acid being 90 and the total acid 108. Barium gastrointestinal studies showed a normal stomach with no six-hour residue, a constant irregularity of the duodenal cap and a normal intestinal tract. A very small diverticulum at about the junction of the middle and the lower third of the oesophagus was noted, probably due to traction on the gullet at that point by a mediastinal adhesion due probably to an old mediastinitis. He was given careful dietetic and alkali-

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\*Clinic before the American College of Physicians at the Peter Bent Brigham Hospital, Boston, April 11, 1929

line treatment on the medical service for a little more than a month with considerable relief but curiously enough when enough alkaline powders were given to control his acidity his gastric motility was interfered with and there was definite evidence of hypersecretion. Although his acute pain was improved he continued to have soreness and discomfort. My colleagues felt that medical treatment at home would be even less satisfactory and that he should be offered a surgical operation, in which opinion I concurred.

Operation was done on January 6, 1928, under ether anaesthesia. The stomach was normal, the pylorus patulous. All the other viscera including the appendix were normal. Just beyond the pylorus the duodenum showed a characteristic puckered, stippled and slightly thickened area. It was determined to resect the pylorus and as much of the first part of the duodenum including the ulcer as possible. The antrum of the stomach was divided just distal to the incisura, the dissection carried down behind the first part of the duodenum and the bowel sectioned as far distal as possible, still leaving room enough to turn the end in. This dissection was carried through adhesions between the duodenum and pancreas which indicated that the ulcer was posterior and somewhat penetrating. A direct anastomosis of the open end of the stomach to the jejunum behind the colon was made with cat gut sutures. Recovery was uneventful. Pathological examination showed that the section of the bowel had passed through the edge of a practically healed ulcer. It seemed clear, therefore, that the treatment had

caused at least a temporary healing of the ulcer and that the latter had been completely removed or if not that at least any remaining ulceration was entirely excluded from the gastric contents. X-ray studies on discharge showed that the barium passed rapidly through the stoma.

The patient was at first completely relieved of his symptoms but some months later developed distress without relation to meals but always relieved by powders. Nearly eight months after the operation he had several tarry stools and felt weak, and was readmitted to the hospital on the medical service on August 24, 1928. On this occasion he showed no anemia in spite of the hemorrhage. More x-ray studies showed a rapid emptying of the stomach without visible peristalsis, no six-hour residue and no demonstrable tenderness, spasm or craters. It was reported as showing no evidence of ulcer.

On this occasion he was kept nearly two months in the hospital under medical treatment. The stools, at intervals, showed traces of blood but on the whole he improved symptomatically and was discharged on October 16, 1928, with a red cell count of 5,840,000 and hemoglobin of 90%.

The third admission to the medical service occurred two months later because although the patient had been pretty comfortable during the interval he had several large tarry stools and a serious attack of weakness. On this occasion his blood showed a moderate secondary anemia but again both general physical and x-ray examinations showed no evidence of ulcer. Needless to say a search for some other

bleeding point in the alimentary tract was conducted with great thoroughness but was negative. The question of the possible responsibility of the little diverticulum of the esophagus was constantly in the minds of his advisers but it was not considered important for the reason that he had no symptoms referable to the lesion and never vomited blood. I saw him in consultation on this occasion and was encouraged by my colleagues to consider the performance of a subtotal gastrectomy but in the utter absence of evidence of any lesion of the stomach, or indeed elsewhere, I was unwilling to operate. The patient remained in the hospital for about six weeks and was discharged relieved. His fourth admission was to the medical service less than one month afterward and was the result of another much more severe hemorrhage from the bowel with marked faintness and pronounced secondary anemia, the red count getting as low as 2,000,000 and hemoglobin 30%. Now, more than six weeks after this admission he is still in the hospital. It has been slow work on this occasion to build up his blood; yesterday we made another barium x-ray examination which showed a perfectly normal stomach, emptying promptly into the distal loop of the jejunum. A little of the barium passes into the proximal loop but does not tend to pass backward into the duodenum. No crater can be made out and no tenderness to pressure. The normal rugae of the stomach can be beautifully demonstrated under the fluoroscope passing down to the point of anastomosis without modification of their arrangement. There is not the

slightest evidence of ulcer. Gastric analysis shows a fair acidity on the fasting contents and a maximum acidity on the withdrawal of the fourth specimen of 55 free acid and 72 total acid.

Now, what are we to think of this patient? It seems fair to say that medical treatment has been a total failure. No doubt if the patient could have given up any form of activity and remained hospitalized and fed on slops and powders he could have been kept fairly comfortable and possibly the hemorrhages would have been averted, but it is hardly reasonable to expect that a patient should submit to such treatment continuously for sixteen months. The patient states on close questioning that since the operation of January 6, 1928, he has been free from the old ulcer pain which was so severe and that the discomfort which he usually complains of now is of a different sort, situated in a different place and is not very severe. He feels that if it were not for the hemorrhages he would be able to carry on his vocation and would be well satisfied. It may be said, therefore, that the operation has to a considerable degree relieved symptoms and has somewhat reduced the acidity but the hemorrhages which jeopardize his life certainly make it necessary for us to adjudge the surgical treatment also as a failure.

Let me leave Bennie Wean for a moment and discuss certain general impressions which have been crystallized in my mind during the years in which I have been trying to accomplish something with peptic ulcer. As to the etiology of the condition my

impressions are chiefly of a negative sort. Many, but not all, of these patients are of "nervous" or high-strung temperament, many, but not all, among the men, are excessive cigarette smokers, many, but not all, carry burdens of worry or anxiety, many, but not all, have bad teeth and some have infected tonsils. In every patient upon whom I have operated I have made it a point when possible to examine all the abdominal viscera and usually to remove the appendix. I have never observed the incidence of appendicular lesions with any more frequency than would have been the case in an equal number of abdominal sections made for other purposes. I have not noted any association with cholecystitis and therefore I cannot consider the theory of focal infection from these sources at all seriously. The theory of emboli of the arterioles of the stomach and duodenum with resulting necrosis and digestion of tissues has not impressed me, for I cannot see why these patients who are so often young and otherwise healthy should have emboli in this particular locality and never show evidences of emboli elsewhere. It is quite true that small emboli in most organs might be without symptoms but certainly they should sometimes strike in places where the symptoms would be equally or more serious than in the case of the upper alimentary tract. The one striking fact which has always been emphasized in ulcer cannot be excluded, namely, that the overwhelming majority of ulcers occurred in a limited area along the lesser curvature of the stomach antrum and the first portion of the duodenum and that this area is precisely where

traumatism is most likely and where hyperacidity is greatest. The partially masticated food when ingested lies at first in the proximal and middle portions of the stomach rather inertly and for a considerable time retains its alkalinity derived from the saliva. It is true that the acid secretion is derived chiefly from the glands in the pars media of the stomach rather than in the antrum but the acidified chyme is gradually pushed down into the antrum where it is subjected to the extremely vigorous churning peristalsis of that portion of the viscus. It seems reasonable to believe that a combination of vigorous muscular action and poorly masticated food may result in trauma to the mucosa—a trauma which at once leads to auto-digestion by the strongly proteolytic acid gastric juice, the same is true of the first portion of the duodenum where chyme of the same character is pounded by the action of the sphincter and the vigorous peristalsis of the first part of the duodenum. Once the chyme passes from the first into the second portion of the duodenum its acidity is neutralized by the bile and pancreatic juice and by the same token we cease to meet (with negligible exceptions) with spontaneous ulceration.

Naturally, other factors almost too numerous to mention enter in. If a patient has abscessed teeth and a foul mouth it is likely that the food is but little masticated and more likely to cause trauma. If he is worried and anxious and depressed over his inability to pursue his vocation and earn a proper living for his family it is likely that his gastric glands will be stimulated to increased secretion. Preu-

mont's observations more than one hundred years ago of the influence of the emotions on the gastric secretions as observed through the fistula of Alexis St. Martin are as sound now as when they were first reported. Once an ulcer has formed at or just beyond the pylorus its irritation causes pylorospasm, retention and therefore increased secretion. Perhaps this influence is exerted by those legendary messengers "Hormones."

We are justified in conceiving of frequent minor traumatism of the mucosa with slight auto-digestion of the devitalized tissue causing slight erosions which result in heart burn and discomfort but are promptly and completely repaired by the healing processes. In a certain instance, however, the traumatism may be more severe, the auto-digestion more intense, and the struggle between the proteolytic and reparative processes waxes and wanes with success attending first one and then the other until finally chronic inflammatory changes take place in the wall of the viscus at the disputed point with increasing fibrosis, contraction of the tissues about the arterioles and consequent starvation of the ulcer, rendering it relatively devitalized and more easily attacked by digestive ferments. Thus is formed the chronic indurated peptic ulcer.

Medical treatment which aims to correct hypersecretion by rest and diet, to relax pylorospasm, and to neutralize the acid by chemical means is logical and rational. That it usually secures permanent healing in early cases is undoubted; that it relieves symptoms if it can be consistently pursued is certain; but in the case of the

chronic indurated ulcer how often does it cure in the sense of restoring the patient to a condition where he is not more liable to a recurrence of ulcer than is a normal individual to develop the lesion *de novo*? Very seldom, according to my belief. As I have observed my friends who have been successfully treated for ulcer, by medical methods, they appear to me to have one eye on their diet and another on the bicarbonate of soda bottle, and to be usually trying to avoid fatigue. They seem to be rarely more than two jumps ahead of the ulcer! And this is the situation among those who can afford to live at a reduced level of activity and to take care of themselves. Can the average patient, as we meet him in hospital and office practice, afford to pay to his ulcer the tribute demanded in terms of enforced inactivity, special diet and medicine with all the disadvantages which these measures entail? No doubt some patients may be symptomatically cured of their chronic ulcers by a careful course of medical treatment but I personally believe this to be uncommon. Much more common is the patient who can be set on the right track by medical regime and may then keep himself comfortable by habitual selection and limitation of diet, by diminishing his vocational and other activities, by enforced rest and occasional alkaline medication. All too common is the large group where the price paid for reasonable comfort is eternal vigilance, habitual renunciation of both wholesome work and of many pleasures, strict diet and constant medication. The average man has not the means or self-control to carry out these measures, therefore,

he muddles along between periods of physical misery with nervous depression and of comparative well-being bought at the price of self-denial and inactivity which may bring his family face to face with want, and a certain small percentage of these patients will die of acute perforation or hemorrhage unless saved by an emergency operation

Surgery proposes a method of treatment as rational and logical as that offered by medicine, and based on the same underlying principles though accomplished by mechanical measures. It can remove the ulcer or segregate it from the acid gastric contents, it can do away with pylorospasm and secure more rapid emptying of the stomach, hoping thus to diminish hypersecretion and hyperacidity, it can do away with obstructing cicatrices which interfere with motility. The price it exacts is a small operative mortality and the discomforts and complications attending operations in general. Its results (excluding the fatalities and certain rare complications) at their worst are no more evil than failures in medical treatment. At their best they are superior, on the whole, to the results of the medical management of obstinate chronic cases which are the only ones (barring the acute perforations) which should be operated on. It is the misfortune of surgery that its failures excite more criticism and disparagement than those of medicine because of the ordeal to which the patient is submitted,—an ordeal, by the way which is often much exaggerated.

Let us review briefly the types of procedure and of the advantages and disadvantages which they offer, con-

sidering first duodenal ulcer which is by far the most common form. Gastro-jejunostomy is the simplest and safest procedure. If it succeeds in diverting the whole of the acid chyme from passing through the pylorus and in causing a prompt emptying of the stomach, it secures the two great desiderata—segregation of the ulcer and diminution of secretion and is likely to give a brilliantly successful result. Unfortunately there can be no assurance that the new stoma will function perfectly, almost always if the pylorus is patent some of the chyme will pass through this normal channel and attack the ulcer, and secretion will not necessarily be diminished. Moreover, the point of union of stomach with jejunum may offer a point of diminished resistance where a new ulcer may form. In spite of these disadvantages gastro-jejunostomy is the most practised procedure and gives many excellent results.

Resection of the ulcer with a simple plastic operation on the pylorus after the Heineke-Mikulicz plan is feasible only if the ulcer is situated anteriorly and is likely to be unsatisfactory because it appears that secondary contraction of the scar is apt again to narrow the pylorus and cause retention and hypersecretion. A more elaborate type of pyloroplasty by the Finney method is more likely to succeed, though here again, if the ulcer is to be excised we are limited to those situated anteriorly and in some cases also restoration of pyloric function and spasm may occur. Nevertheless this method in our hands has given some brilliant results.

Exclusion of the pylorus by some form of plication or ligation, with gastro-jejunostomy, rarely succeeds since the lumen usually restores itself. Complete exclusion of the ulcer, or better still its extirpation, with some measure to promote rapid emptying of the stomach, seem to me to offer the most logical plan and in this opinion I am supported by an indication given by Nature herself, for it is widely admitted that a duodenal ulcer which has resulted in cicatricial closure of the pylorus is most favorable for permanent cure by gastro-enterostomy. Why may we not imitate this by surgical exclusion? The pyloric antrum is transected vertically at the incisura, the dissection is carried behind the pylorus and first portion of the duodenum as far as possible and the bowel divided beyond the ulcer. A direct anastomosis may then be made, if the structures are mobile enough, between the open end of the stomach and the duodenum,—a method frequently called the Billroth No. 1. Thus it is assured that the gastric contents will be propelled by the normal peristalsis in its accustomed course and the absence of the pyloric sphincter mechanism should promote rapid emptying of the stomach. If the direct anastomosis to the duodenum is not feasible, the stomach may be anastomosed to the jejunum either by its already open end (Polya) or by closing the opened end and making a posterior gastro-jejunostomy, which I believe to be the preferable method. If, as frequently happens, the penetration of the posteriorly situated ulcer into the substance of the pancreas makes it impossible to resect the duodenum the divided antrum is closed

by suture, which, of course, effectively segregates the ulcer from the acid chyme, and the operation is completed as before. It is my present belief that a completely excluded ulcer will almost invariably heal. This method appears to have given many most satisfactory results. I have not been able to approve of the subtotal gastrectomy for duodenal ulcer, as in spite of favorable statistics I believe that it is likely to entail an excessive mortality and also that it is undesirable to impair so seriously the useful, if not absolutely essential, function of the stomach.

How shall we select the operative procedure to be used? I believe that the resection or total exclusion type of operation should be considered the ideal and should be employed if possible, but if the local conditions found make it too difficult technically to carry out with comparative safety, it should be abandoned and a simpler operation, usually a gastro-jejunostomy, carried out. If the patient is very adipose or in any other way an unfavorable subject, gastro-jejunostomy should be the operation of choice and in experienced hands ought to be almost free from mortality. We must be content to do something less than the theoretically ideal inasmuch as we are not dealing with a progressively fatal disease but one in which the operation may usually be considered highly expedient rather than absolutely necessary.

Turning for a moment from duodenal to the far less common gastric ulcer the same general principles may be said to apply. Resection of the ulcer with gastro-jejunostomy to promote rapid emptying of the stomach is

the operation of choice but often the ulcer is so situated or so extensive that the surgeon will be forced to carry out a more extensive attack with resection of a considerable portion of the stomach and appropriate restoration of gastro-intestinal continuity, very likely by ante-colic direct anastomosis of the jejunum of the Polya type. Here, again, if difficulties are encountered or the patient is not a good subject, the surgeon should be content merely with a gastro-enterostomy, for I am very decidedly not one of those who believes that a primary peptic ulcer is often the starting point of carcinoma.

It is hardly necessary to amplify what I have said in defining my attitude toward ulcer by emphasizing what all physicians and surgeons alike are agreed on, namely, that acute perforation, persistent recurring bleeding and cicatricial contractions causing serious motor disturbances require surgical measures for their attempted relief.

Let us now return to this patient, Wean,—he is the first who has apparently completely disproved my contention that a completely excluded ulcer will heal, but since we can find no other source of his hemorrhage, even though the ulcer has been nearly completely resected and excluded, we must assume that the bleeding is from the same source. He presents indeed a serious problem. It is clear that we cannot conscientiously trust or hope that these hemorrhages will now stop spontaneously. We must explore and I have the impression that our examination of the stomach, the anastomosis and the afferent and efferent limbs of the jejunum will fail to show

externally any evidence of a new ulcer. We must then examine the duodenal stump, and, buried as it is in scar tissue, underneath the liver and in relation to the bile ducts and head of the pancreas, I doubt very much whether we can get by inspection or palpation any reliable evidence of ulcer. Nevertheless, I shall be in favor of freely opening the duodenum in order to make absolutely certain of the condition. If an ulcer is found, it will probably lie directly upon the gastro-duodenal artery or one of its main branches in relation to the head of the pancreas. I think the further procedure will present a serious problem but I hope that it may be possible to excise still more of the duodenum, with or without ligation of the artery. The trouble is, of course, that the anastomoses of this vessel with pancreatic or duodenal branches from a different source—the superior mesenteric—are so free that we cannot expect too much from ligation of a single trunk. I should feel at any rate that the only possible effort will have been made to repair a lesion which is likely to be fatal if something cannot be accomplished.

Let me show you for a moment this other patient, Abraham Fine, who represents about what I have learned to expect as the immediate result of these operations. He is also a young Russian Hebrew who developed ulcer symptoms about two years ago, was diagnosed and treated medically first in the wards and then in the excellent special clinic of the Massachusetts General Hospital obtained only partial relief and was finally advised to have an operation when a full year



refused. His misery continued, he was unable to work, his anxiety about his wife and family became acute and when he fell into my hands he was anxious to accept the possibility of operative relief. X-ray showed a typical duodenal deformity with slight gastric stasis. At operation the antrum was divided, resection found impossible on account of penetration into the pancreas, the ulcer completely excluded by closure of the antrum and a posterior gastro-jejunostomy made. Here he is now completely free of symptoms, and rapidly regaining his strength. He states that from the moment he recovered sufficiently from the anesthetic to analyze his feelings he has not experienced a moment of the old ulcer pain. He is on a six-meal diet of milk, cream, cereals, toasted bread, eggs, orange juice and occasionally a little chicken. Barium x-ray studies made yesterday show that there is no residue, the ingesta passing rapidly down through a satisfactory stoma into the distal loop. Gastric analysis has not been made but there is very good reason to believe that secretion has been much diminished. Were it not for the case of Benne Wean I would say with much confidence that the excluded ulcer will heal and remain permanently out of the picture. In spite of this disappointment I think that Abraham Fine, if he takes reasonable care of himself, can lead, without discomfort, an active and useful life and support his family.

It would be easy to pack the floor of this amphitheatre with old patients illustrating the successful surgical treatment of ulcer but I think it would add nothing to this demonstration because you and I both know that it could be packed also with the unsuccessful examples of surgery and with the successes and failures of medical treatment. I have intended to be, and I hope that I have given you the impression of being entirely candid in the expression of my views. The successful handling of a patient with ulcer depends not upon rigid adherence to one viewpoint but on willingness to recognize the usefulness of different forms of treatment and to select and apply with skill and patience that method which is best adapted to the individual patient. The best criterion of sincerity is the course chosen by the physician himself if he were afflicted. I am quite clear in my mind that if I were so unfortunate as to have a peptic ulcer I would take a prolonged vacation and put myself in the hands of my medical colleagues for careful and rigid treatment, that I would then resume reasonable activity with moderate dietary restriction and if I had another exacerbation I would repeat the process, if then, I found that I could not pursue a reasonably active and useful life and that I must submit to irksome and distasteful dietary restriction and medication for an indefinite time, I would gladly turn to any relief which surgery might offer.

# The Suprarenal Glands and Hypertension:

## A Study of the Veins Within the Suprarenal Glands\*

By EDGAR V. ALLEN, M.D., *Fellow in Medicine, The Mayo Foundation, Rochester, Minnesota*

IN 1855 Addison described a clinical syndrome due to disease of the suprarenal glands. In his description there is a hint of the physiologic relationship between these glands and the cardio-vascular system, for he found "the pulse, perhaps, large but remarkably soft and compressible" and "remarkable feebleness of the heart's action." In the opening paragraph of his thesis Addison said in part, "The functions of the suprarenal capsules are almost or altogether unknown" and "I am not aware that any modern authority has ventured to assign to them any special function or influence whatever."

In the seventy-three years that have passed since Addison's statement, numerous contributions on the suprarenal glands have served steadily to increase the large store of information which was so obviously absent in Addison's day. Only the most important contributions, and those pertinent to this paper, can be mentioned here. They are (1) death follows promptly and characteristically after removal of both

suprarenal glands (Brown-Séquard, 1856), (2) the aqueous extract of the medulla of the suprarenal glands has a distinct action on the blood vessels and heart, causing vasoconstriction and raising the blood pressure (Oliver and Schafer, 1894, and Cybulski and Szymonowicz, 1895), (3) there is a similar substance in the veins of the suprarenal glands (Langlois and Cybulski and Szymonowicz, 1897, and Dreyer, 1899), (4) isolation of the actual principle (epinephrine) of the medulla of the suprarenal gland (Abel, 1899), synthetic preparation of this substance designated suprarenin (von Furth, 1900), (5) stimulation of splanchnic nerves causes increased secretion of epinephrine (Dreyer, 1899), (6) independent isolation of the active principle of the medulla of the suprarenal gland, called "adrenalin" (Aldrich and Takamine, 1901), (7) epinephrine produces the same effect on certain structures as direct stimulation of splanchnic nerves (Lewandowsky, 1900), and (8) the confirmation of von Furth's work (Dakin, 1905). In the early period of investigation of the function of the suprarenal glands it was believed that epinephrine was the product of the medulla only and that the adrenal cortex was not for its

\*Abridgement of thesis submitted to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the degree of Master of Science in Medicine, 1928.

However, Biedl<sup>6</sup> and Wheeler and Vincent demonstrated that fishes and other animals could live if deprived of all the medullary tissue of the suprarenal glands. This implied that epinephrine was not essential for life but Kohn<sup>30,31</sup> showed a chromaffine substance like that in the medulla of the suprarenal gland, in other situations, Fulk and MacLeod presented evidence that the active principle of the retroperitoneal chromaffine system has the same physiologic action as epinephrine, and Hartman demonstrated the presence of epinephrine in the cortex of the suprarenal glands.

The value of epinephrine to the normal organism is controversial. Stewart and Rogoff showed that the spontaneous liberation of epinephrine was abolished as far as could be determined by section of both sympathetic trunks and that cats survived indefinitely the removal of one suprarenal gland and section of the nerve supply to the remaining gland. Gley maintained that epinephrine is not of physiologic significance and is probably a product of waste or excretion, Stewart believes it is a relic of some remote phylogenetic epoch, that all functions of the suprarenal gland are dependent on the cortex, and hence that clinical syndromes of suprarenal insufficiency are purely inventions of clinicians of uncurbed imagination. These views are vigorously combated by Pende, who brings to his support the work of Roux and Taillander, Marshall and Davis, Hartman and Blatz, Hartman, Cannon, Cannon, Udill and Griffith, and others.

In view of the opposed opinions of these protagonists and antagonists concerning the value of epinephrine, a

middle path only can safely be pursued. Two facts are obvious: the suprarenal glands are essential for life and they produce epinephrine, which is capable of provoking widespread vasoconstriction and increase in the arterial blood pressure. It has not been proved that epinephrine is necessary for the maintenance of normal vascular tone and blood pressure.

Seventy-three years of observations and investigations have not brought certain problems regarding the rôle of epinephrine in the normal organism to an acceptable conclusion. Its status in hypertension is equally chaotic, for, as Mosenthal has said, "This idea (epinephrinemia as a cause of hypertension)\* has been categorically affirmed and denied." My study, which is purely one of morphology, is presented with full recognition that a physiologic interpretation on such a basis is extremely hazardous, but according to Cannon "It is too bad that the separation of histology from physiology has become so sharp."

Morphologists have long been aware of the well developed musculature of the veins of the suprarenal gland. Attention has been called to the distribution of this musculature in masses running longitudinally to the axis of the vein, a unique arrangement when contrasted with musculature of veins elsewhere in the body. The absence of circular muscle in the central vein and tributaries has been noted. Henderson and Goldzieher and Sherman have reviewed the literature essential for an understanding of this musculature, and the former demonstrated it by actual

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\*Parenthesis and contents mine

reconstruction Without doubt, many students of pathology have noted differences in volume of the muscle masses in the veins of suprarenal glands removed at necropsy in cases of normal and high blood pressure Robertson has observed this condition over a period of twenty years and this paper is an outgrowth of a suggestion made by him Accurate estimations of these differences have been lacking

#### MATERIAL AND METHOD

The tissue used for study had been removed at necropsy and preserved in solution of formalin Many of the glands had been cut in two or more sections for routine study All pieces of any considerable size were sectioned provided they contained one pole of the gland No attempt was made to differentiate right and left glands Sections were cut approximately 1, 2, 3 and 4 cm from either end of the gland, through a line perpendicular to the convex surface These sections were numbered 1, 2, 3 and 4 in each piece of tissue studied, depending on the distance from the pole of the gland (fig 1)

Glands from two groups of cases were studied those of so-called essential hypertension, and those of normal or low blood pressure From the latter group were excluded all cases of primary cardiac disease and myocardial degeneration, nephritis, brain tumors, injuries with shock, hyperthyroidism, fever from any cause, myxedema, jaundice, emaciation or exhaustion from any cause, and hypertrophied prostate gland, as these conditions might influence the blood pressure unduly The group included the glands from patients who had died as a result of operation for carcinoma, chronic ulcerative colitis, progressive bulbar palsy, pregnancy with hemorrhage, intestinal obstruction chronic cholecystitis with stones and diaphragmatic hernia The average blood pressure, in millimeters of mercury, in the hypertension group was 200 systolic and 110 diastolic the average age was fifty-four years The average blood pressure in the normal group was 126 systolic and 78 diastolic the average age was forty-eight years Sixty-eight sections from eighteen cases of known hypertension and fifty-seven sections

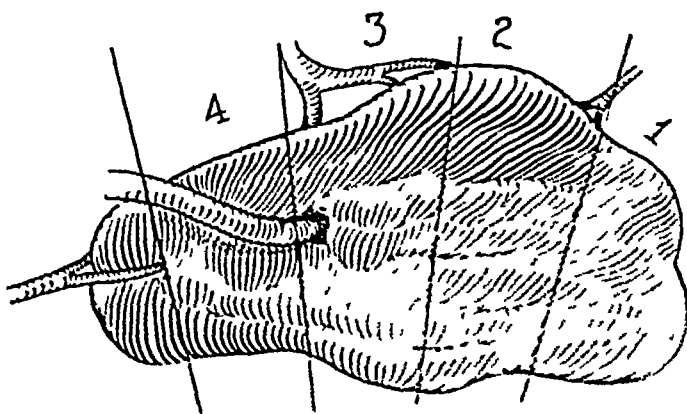


FIG 1 The method of cutting each gland into sections

from twenty-five cases in which the blood pressure was normal serve as the basis of this study. The tissue was imbedded in paraffin and stained by Weigert's elastic-tissue and van Gieson's connective-tissue stain. The former aids in the identification of arteries, the latter of muscle.

The problem of identifying veins and excluding arteries was immediately apparent on microscopic examination. The following standard for identification was adhered to (figs 2 and 3)

#### ARTERIES

Walls of uniform thickness  
Circular lumen  
Circular muscle present  
Longitudinal muscle regularly distributed  
on all sides of the vessel  
Internal elastic lamina present

#### VEINS

Walls of greatly varying thickness  
Irregularly shaped lumen  
Circular muscle absent  
Very irregularly distributed longitudinal muscle  
Internal elastic lamina absent

Vessels with an actual maximal outside diameter of less than 0.4 mm were not measured, and if the maximal actual thickness of the muscle of any vein was less than 0.06 mm, it was considered to be without musculature. Throughout this paper, the term "veins without muscle" applies to this group, and to those veins actually without muscle. All vessels without muscle and with diameters in excess of the minimum for measurement were considered veins, although many of them were doubtless endothelial lined sinuses connecting the arteries and veins. All veins so chosen for study were projected on ordinary white paper and drawn at magnifications varying from

25 to 200 times. These drawings were then measured with the planimeter, an instrument which provides such an excellent means of calculation in this type of work that it is surprising it has not been more extensively used. It consists essentially of a fixed mass with a pivoting arm which fits into a socket. This socket may be moved back and forth on a bar which has, at one end, a pointer with a finger grip, on the other end is a double scale by which calculation may be carried to the third decimal place (fig 4). At the beginning of any piece of work the movable socket is fixed on the bar by a screw, thus preventing changes in the distance relationship to the scale and the pointer. The value of 10 on the scale must be determined. The following will illustrate how this determination is made. A primary reading of, for example, 1165 is made, the pointer is moved around the circumference of a known area of 100 sq cm and a second reading of 2365 is taken. The difference between the first and second readings constitutes the final figure, 12. Then the value 12 on the planimeter scale equals 100 sq cm of surface area and the value 10 equals 83.33 sq cm ( $12 \div 100 \times$ ). Subsequently the absolute surface area of projected images can be determined with accuracy by multiplying the final reading on the planimeter scale by 83.33. The calculated constant will change with changing conditions. Marked irregularities in the outline of areas measured do not constitute an obstacle to accuracy if the planimeter is used.

In each vein with muscle, the area included within the maximal circum-

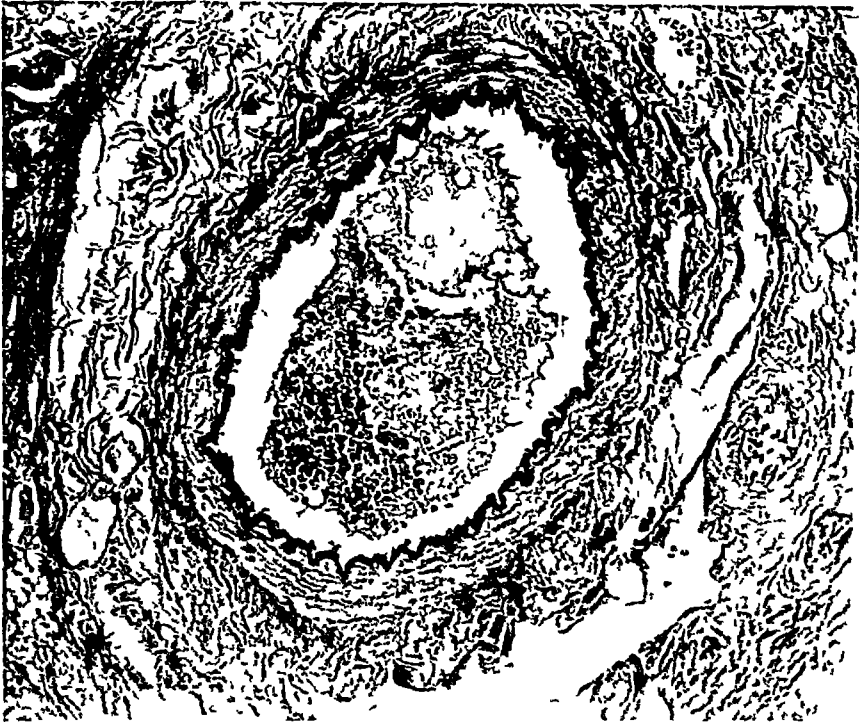


FIG 2 Weigert stain of an artery in the substance of the suprarenal gland, showing the circular lumen, the regularly distributed musculature and the internal elastic lamina (X 110)





ference of the vein and its muscular wall was calculated, the second estimation was of the area of the lumen, the difference between the first and second figures was considered the area of the muscle. More than 1300 such measurements were made in this study of approximately 750 veins. After the areas of the lumen and of the muscle of the projected image is known, the absolute area is determined by dividing by the magnification. The ratio of muscle to lumen of any vein is calculated by dividing the absolute area of the muscle by the absolute area of the lumen.

In order that a comparison might be made of the veins removed from the same areas in the two groups, the number 1 section of the hypertension group was compared with the number 1 section of the normal group, the number 2 section of the hypertension was compared with the number 2 section of the normal group and so forth. For comparison of veins of equal size, they were divided into groups depending on the absolute area of their individual lumens regardless of their situation in the gland as follows:

Group 1	Less than 10 sq mm
Group 2	100 to 199 sq mm inclusive
Group 3	200 to 299 sq mm inclusive
Group 4	300 to 399 sq mm inclusive
Group 5	400 to 499 sq mm inclusive
Group 6	500 to 599 sq mm inclusive
Group 7	600 to 699 sq mm inclusive
Group 8	700 to 799 sq mm inclusive

Larger veins were grouped according to the foregoing system.

#### OBJECTIONS TO THE METHOD

The method of estimating the ratio of musculature to lumen by measuring

diameters of the lumen and thicknesses of muscle is open to much criticism. This is particularly true in measurements of the musculature and lumens of the veins of the suprarenal gland, in which the lumens and masses of muscle are extremely irregular in diameter and thickness (figs 3, 5, 6, 7). These irregularities make the method of measuring diameters of the lumens and thicknesses of the walls inaccurate and impractical. Even in vessels in which the lumens and the distribution of muscle are regular, this method does not give information of the actual ratio of the total mass of muscle surrounding the vessel to the area of the lumen, but only the ratio of the thickness of the muscular wall to the diameter of the lumen.

The use of the planimeter obviates all error of determination of the relative sizes of lumen and musculature as represented in the projected drawings, regardless of the irregularity of the lumens or of the masses of muscle. It does not, however, influence the error in the manner of study previous to and including the drawing of the projected image of the vessel. These errors are present in all methods. Three factors interfere with absolute accuracy: (1) it is impossible to cut sections from the suprarenal gland exactly at right angles to the convex and flat surfaces; (2) the veins pursue an irregular course through the substance of the gland and are thereby cut at many angles; and (3) it is sometimes difficult, even with the van Gieson stain to determine at what point musculature terminates and surrounding fibrous tissue begins. This is particularly true in sections in which





FIG 5 Vein from a suprarenal gland in a case of hypertension, showing the enlarged longitudinal muscle masses (X 100)

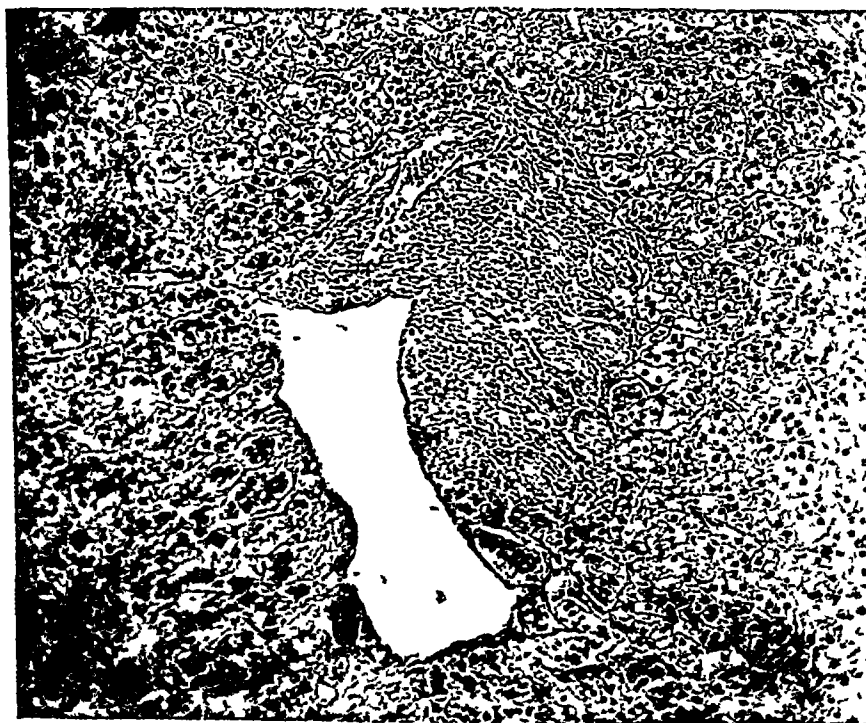


FIG 6 Vein from suprarenal gland showing marked hypertrophy of the muscularis in a case of hypertension (X 100)

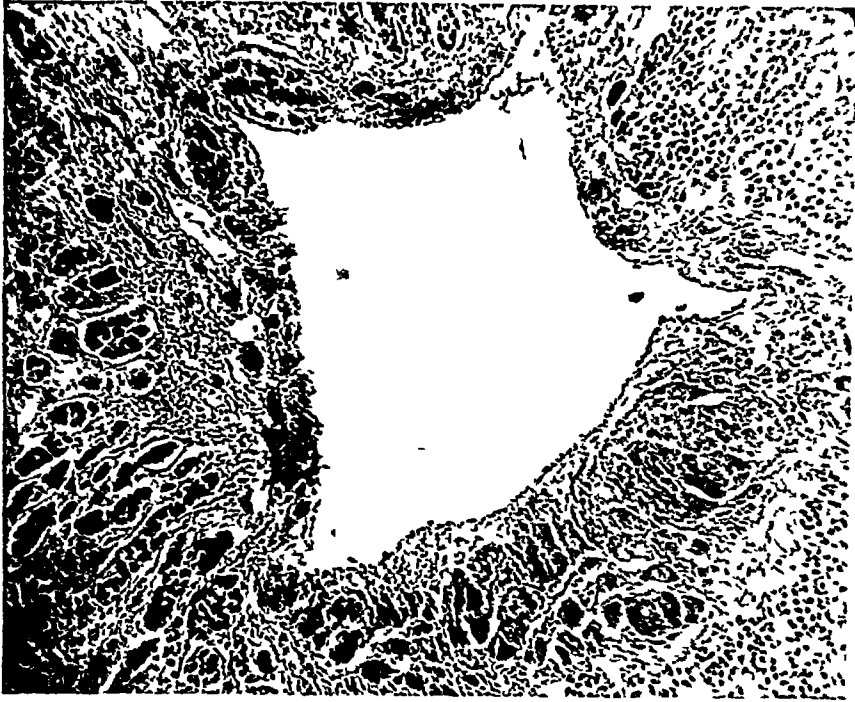


FIG 7 A vein from a suprarenal gland in a case of normal blood pressure. The cross section area of muscle is comparatively small when compared with the cross section area of the lumen (X 75)

isolated bits of muscle are found separated from the muscle, and in those in which the fibrous tissue pushes in around the outer edge of the muscle. Since there seems no way to obviate these difficulties, they must be borne in mind, but must be considered common to both groups studied. The method of measurement with the planimeter, even with its limitations, is vastly superior to other methods for determining the relative sizes of vessels and their walls.

#### RESULTS

*The muscle-lumen ratio.* The ratio of muscle to lumen of veins of the suprarenal glands in cases of hypertension can be accurately compared with the ratio of muscle to lumen in cases of normal blood pressure only if vessels of comparable size are

studied. For this purpose, all veins with musculature were grouped according to the area of the lumens, as described. Veins of the suprarenal gland in which the individual actual area of the lumens is in excess of 299 sq mm, are rare in cases in which the blood pressure is normal and for the purpose of comparison of the ratio of muscle to lumen in the hypertension and the normal groups, all veins with a lumen area in excess of 299 were considered in group 4. The results of this study are shown in table 1 and figure 8. As the lumens increased in size in the veins of patients whose blood pressure was normal the total mass of muscle relatively decreased. The veins of the patients with hypertension with areas of lumen less than 200 sq mm showed the

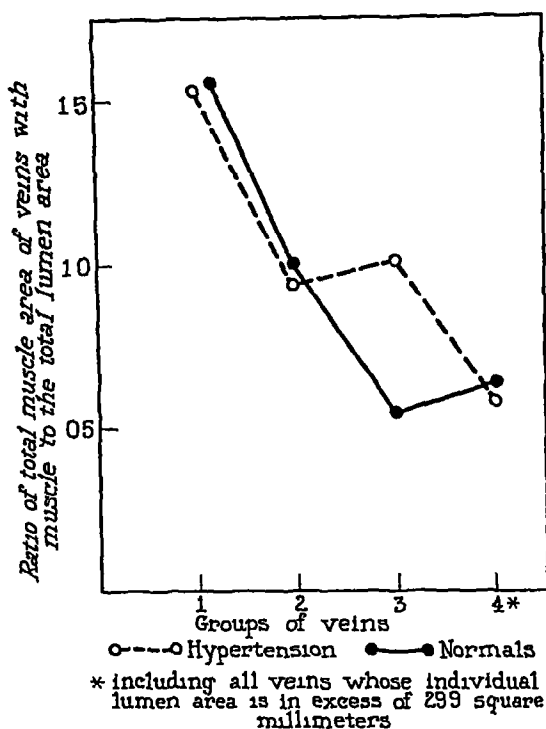


FIG 8 Comparison of the ratio of muscle to lumen in cases of normal and high blood pressure. This ratio as compared with the normal is approximately twice as great in veins of group 3 in cases of hypertension. In the ratios, which are expressed as single values, the unexpressed quantity is understood to be 1. That is, the highest ratio would read 1.5 to 1.

same decreasing proportion as the veins become larger. Hypertension veins of group 3, however, deviated markedly from the normal, and instead of the amount of muscle in proportion to the lumen decreasing, it actually increased (figs 5 and 6). Whereas, in the group 1 veins, the 1.5\* ratio of hypertension veins compared favorably with 1.5 ratio in normal veins and the 0.87 ratio of the hypertension veins of group 2 compared favorably with the 0.97 ratio of the normal veins, the 0.99 ratio of the hypertension veins of group 3 was almost double the 0.57 ratio of muscle to lumen in the normal

veins. This is excellent evidence that the hypertension veins of group 3 have marked hypertrophied musculature. This difference disappears in the veins of group 4 as the ratio of muscle to lumen of the normal group is 0.65 and compares favorably with the ratio in the hypertension group, which is 0.59 (table 1, fig 8).

While this work was in progress, an article by Goldzieher and Sherman on the same subject appeared. They calculated, by measurement of diameters of the lumens and thicknesses of wall, the ratio of lumen to muscle in cases of hypertension and in cases of known normal blood pressure in fifty-one cases, selecting nine veins from each. They said, "The musculature of the suprarenal veins in cases of hypertension compares with that of the supra-

\*By this expression is meant that the ratio was 1.5:1 and in each instance in this paper in which ratio is expressed by a single value it is understood that the other quantity, although unexpressed, is 1.

TABLE I

RATIO OF AREA OF MUSCLE TO AREA OF LUMEN IN SUPRARENAL VEINS IN CASES OF ELEVATED AND NORMAL BLOOD PRESSURE

	Group 1	Group 2	Group 3	Groups 4
	Lumen areas in sq mm less than 10	Lumen areas in sq mm 10 to 19.9 inclusive	Lumen areas in sq mm 20 to 29.9 inclusive	to 9 and 13 Lumen areas in sq mm greater than 29.9
Blood pressure				
Hypertension				
Lumen*	179.5	615.4	983.7	3216.7
Muscle*	286.0	537.4	976.5	1915.8
Number of veins	29	40	40	69
Ratio	1.5	0.87	0.99	0.59
Normal				
Lumen*	339.6	978.0	721.2	573.3
Muscle*	514.0	959.3	412.3	378.0
Number of veins	53	67	29	13
Ratio	1.5	0.97	0.57	0.65

\*Aggregate areas in sq mm

renal veins in cases of normal blood pressure, as 4:1." The variation in the results of their study and of mine is doubtless due to the methods used.

*The total lumen.* Comparison was made of the total lumen area in the hypertension and in the normal groups. For this purpose, the total lumen of all veins with and without musculature was calculated separately in sections 1, 2, 3 and 4 (fig. 1) in each of the hypertension and normal groups. The average was determined in each case by dividing the total lumen area by the number of sections studied. The results are shown in table 2 and figure 9. The hypertension suprarenal glands are markedly more highly vascularized by veins than are the normal glands. Thus, considering the various sections: 1 the average lumen area is 1.8 times as great in the hypertension suprarenal gland as in the normal gland; in sections 2 it is 1.9 times as great, in sections 3, 2.5 times

as great, and in sections 4, 1.6 times as great. One must conclude from these data that the total area of the venous channels, as defined in this paper, in the glands in cases of hypertension was markedly increased over that in the glands in cases in which the blood pressure was normal. A small portion of this increase may be due to the greater size of the glands, as Philpot reported. He studied twelve specimens in one group, five from cases of mild hypertension and seven from cases in which it was assumed that there was hypertension. The average weight of the suprarenal glands was 12.4 gm. There were three specimens in the second group, all from cases in which it was assumed that there was low blood pressure. The average weight of the suprarenal glands was 7.7 gm. These data are entirely inconclusive due to the small amount of material studied. I approached the problem of differences in

TABLE 2

DEMONSTRATION OF INCREASED VASCULARIZATION OF SUPRARENAL GLANDS BY VEINS IN SECTIONS OF GLANDS FROM CASES OF HYPERTENSION AS COMPARED WITH SECTIONS REMOVED FROM SAME AREAS OF GLANDS IN CASES OF NORMAL BLOOD PRESSURE

	Sections 1	Sections 2	Sections 3	Sections 4
Total lumen area in square millimeters				
Hypertension	3230	3111 2	1453 7	325 9
Normal	2262 7	1341 2	468 5	606 8
Number of sections				
Hypertension	28	21	12	3
Normal	37	18	10	9
Average lumen area in square millimeters				
Hypertension	115 3	148 1	121 1	108 6
Normal	61 1	74 5	46 8	67 5
Ratio of average lumen area (hypertension) to average lumen area (normal)	1 8	1 9	2 5	1 6

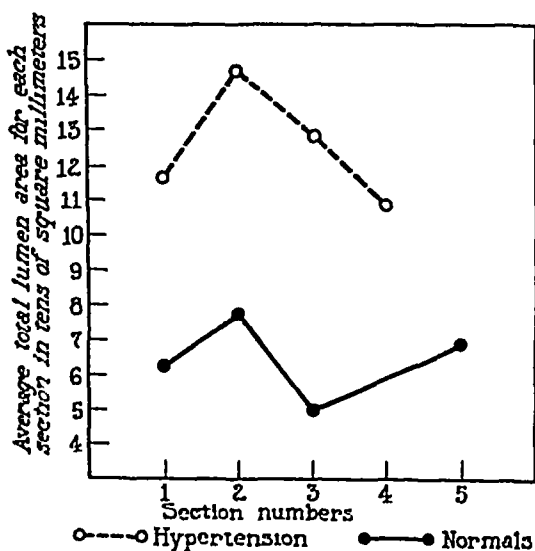


FIG 9 Comparison of the vascularization by veins of sections of suprarenal glands in cases of normal and high blood pressure. The glands in cases of hypertension are more highly vascularized.

the size of glands in the two series of cases by measuring with the planimeter the surface area of the sections studied. There seems no question but that the glands in the hypertension series are larger (table 3). The increased size is, however, entirely inadequate to explain the increased vascularity.

*The percentage of veins with muscle*

Three hundred and thirty veins from cases of hypertension were studied, of these 178 (53 per cent) had musculature as defined in this paper. Of 372 veins from cases in which the blood pressure was normal, 160 (43 per cent) possessed musculature. This series is too small to justify a definite conclusion, but it is probable that the additional 10 per cent of hypertension veins developed muscle—as a reaction to the same factors which produced hypertrophy.

#### ANATOMY AND PHYSIOLOGY

The close connection between the abdominal sympathetic system and the suprarenal glands has been well described by Latarjet and Bertrand. In the main, there are two pedicles, the

posterior and the internal. The former is composed of a considerable number (often more than twenty) of nerve threads. The internal pedicle comes from the solar plexus and is composed of larger fibers which terminate at the lower part of the internal border of the suprarenal gland. The fibers which constitute this pedicle are very numerous. Each suprarenal gland receives not less than thirty-three sympathetic nerve filaments. The close relation of the medulla of the gland to the sympathetic ganglia has been emphasized (Kohn,<sup>10</sup> 1902; Wiesel,<sup>17</sup> 1904, and Biedl,<sup>1</sup> 1913). Elliott<sup>15</sup> has said, "The ganglion cell and the adrenal cell are as brother and sister to one another, born of the same stock, living for the same end in life, which the one attains by growing out into direct contact with the mass of moving muscle, while the other stays quietly where it was born and exercises its influence from a distance."

The blood supply to the suprarenal gland is profuse, it receives from eleven to twenty-one branches from the phrenic accessory, lumbar and renal arteries and some from the ab-

TABLE 3  
COMPARISON OF THE AREAS OF SECTIONS OF GLANDS FROM CASES OF NORMAL  
AND INCREASED BLOOD PRESSURE

	Group 1	Group 2	Group 3	Group 4*
Number of sections				
Hypertension	26	23	13	3
Normal	18	14	9	3
Ratio of average section area hypertension series to normal series	1.3	1.2	1.2	1.4

\*Too few sections to be of value. The glands from patients who had hypertension are larger. The results are vitiated somewhat by irregular shrinkage of the glands.

dominal aorta direct The distribution of blood vessels within the gland has been described by Flint Neumann, Stewart and Rogoff, Burton-Opitz and Edwards have shown that rate of blood flow through the glands is extremely high The results of these various experimenters show a blood flow as great as 7 c c for each gram of organ each minute, or as little as 2.2 c c for each gram of organ each minute, and they give the general impression that the rate of flow is greater than in any other structure of the body Cow demonstrated that blood may pass from the suprarenal gland directly into the kidney and vice versa and suggested that epinephrine may exert some direct control over the kidneys Elman and Rothman demonstrated venous reflux from suprarenal gland to kidney following ligation of the main venous channels away from the suprarenal gland

The increased liberation of epinephrine from the gland, as a result of stimulation of the abdominal sympathetics, has been noted by many physiologists (Cannon and Lyman, Stewart and his collaborators, Dreyer, Tschoboksaroff, and others) Cannon believes the conclusion justified that "the adrenal secretion is under control of the thoracico-lumbar autonomic (sympathetic) system" He demonstrated the effect of emotion on the liberation of epinephrine The pupils of the eyes of a frightened cat became dilated, there is inhibition of movement of the stomach and intestines, increased rate of heart beat and erection of hairs of the back and tail, all of these phenomena are signs of nervous discharges along sympathetic paths,

indicating widespread subjugation of the viscera to control of the sympathetic nervous system. These physiologic reactions may be induced by the injection of epinephrine In fact, epinephrine has been called the mimic of the sympathetic nervous system Cannon demonstrated increased release of epinephrine under conditions of fright He believed that the persistence of the emotional state, after the exciting object had been removed, could possibly be due to the effect of the epinephrine originally released, which had returned to the gland after traveling through the circulation and further stimulating the release of epinephrine Stewart and Rogoff showed that epinephrine was released almost immediately, a fraction of a second, following stimulation of the splanchnic nerves

#### COMMENT

The increased vascularization by veins, as defined in this paper, in cases of hypertension is significant I believe it indicates increased functional activity of the suprarenal glands in cases of hypertension, since there is probably increased vascularization by arteries as well.

The cause of hypertrophy of the musculature of the veins in the suprarenal gland is possibly a subject for conjecture Three chief theories of what the hypertrophy indicates present themselves (1) increased functional activity of the suprarenal gland, (2) increased activity of the general sympathetic nervous system, or (3) a reaction to noxious substances in the blood stream

*Increased functional activity of the suprarenal gland* Although the supra-

renal gland probably secretes products other than epinephrine, the uncertain nature of them makes it necessary to include only epinephrine in this discussion. It should be borne in mind, however, that any other products liberated in the blood stream are subject to the same mechanism to which epinephrine apparently is subject. The mechanism by which epinephrine is expelled from the suprarenal gland is unknown. Neither Cannon nor Rogoff was able to give me information on this subject. The rapidity with which it is released suggests a physical mechanism. As early as 1897, Biedl<sup>1</sup> had shown that the splanchnic nerves convey vaso-dilator impulses to the gland. The longitudinal masses of muscle of the veins in the suprarenal gland have no direct vasoconstrictive effects, because of their peculiar placement. Contraction of these masses would shorten the veins, and probably would increase the diameter\*. This would create an area of temporarily lowered intravascular pressure, into which epinephrine would rush from sinuses containing a high concentration of epinephrine if it can be assumed that such concentrations are present. Surely the time of appearance of increased epinephrine in the venous blood following splanchnic stimulation, a fraction of a second, precludes the more or less passive physiologic extrusion of the product of the cells and indicates that stores of increased concentrations

of the secretion are called on and delivered quickly, probably by some simple mechanism. The contraction of the longitudinal masses of muscle furnishes the most obvious explanation. Goormaghtigh and Elaut, however, believe the suprarenal gland is for emergency function, all the material being stored in advance and the blood routes being ready to augment the exchange surface. Hypertrophy most commonly indicates overwork and there is some logic in the supposition that the hypertrophied musculature in cases of hypertension indicates an increase in the liberation of epinephrine. Goldzieher and Sherman believed, however, that contractions of these muscles in cases of hypertension might occlude the normal channels of venous drainage of the gland and force the venous flow back through the kidney and liver. Its effect might then be primarily on the kidney and secondarily on the systemic blood pressure.

The well known vasoconstrictive effects of epinephrine long ago led to the hypothesis that hypertension was due to hyperepinephrinemia. As early as 1904, Vaquez postulated increase in the function of the suprarenal glands in cases of chronic interstitial nephritis. Aubertin and Ambert, in 1904, examined the suprarenal glands from eight patients who had suffered from contracted granular kidneys, with increased blood pressure, and found hyperplasia or adenoma of the cortex in seven. Josué, Widál and Ménétrier made similar observations. Wiesel<sup>158</sup> made examinations in twenty-two cases of chronic interstitial nephritis with increased arterial tension and long-standing cardiac hypertrophy, in all,

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\*Henderson has shown that when two veins anastomose the bundles of muscle on the adjacent sides fuse in the angle of union. As shown in his diagram, contraction of the longitudinal muscles would produce active dilatation of the vein.



he found hyperplasia of the chromaffin substances in the medulla of the suprarenal gland. Parkinson made examinations in fourteen cases of high blood pressure and found an increase in the chromaffin substances in all but three. Philpot made examinations in twenty-two cases, in nineteen of which the diagnosis had been chronic interstitial nephritis and in three of which hypertrophy of the left ventricle had been present, without chronic interstitial nephritis. He found that the medulla was increased in size and that there was an increased quantity of chromaffin substance. He concluded, "These investigations tend to show that, besides the usual factors associated with, or causing high blood pressure, a condition of increased activity of the suprarenal glands, or hyper-epinephrinism, is very often, if not invariably, present." The finding of increased vascularization by veins in the present study might well indicate increased functional activity of the suprarenal glands in cases of hypertension. Elliott<sup>15</sup> was not of this opinion for in his Sidney Ringer memorial lecture he said, "I could find no justification for the belief that the adrenalin cells are hypertrophied or more active in diseases associated with a persistent increase in blood pressure." Oppenheimer and Fishberg found cortical adenomas in five out of thirty cases of hypertension and only in one out of fifty cases without hypertension. They reviewed the literature and found nine cases of suprarenal tumors, derived from the cortex, associated with hypertension or with cardiac hypertrophy supposedly due to hypertension. From two of the patients concerned

(Volhard), hypernephromas had been removed and the hypertension had disappeared. These authors found in the literature reports of five cases in which there were tumors of the chromaffin substance. In one patient, the tumor was associated with essential hypertension and in one with paroxysmal hypertension, one patient did not have hypertension and two had only anatomic evidence of increased blood pressure. These authors added one case to the few reported in the literature, that of a youthful patient with a blood pressure of 220 systolic and 160 diastolic, in which necropsy revealed a tumor of the suprarenal cortex. Neubauer, Oppenheimer and Fishberg found increased blood sugar in eleven cases with hypertension and felt that this constituted some evidence that the amount of epinephrine in the blood was increased, however, they could not eliminate sclerosis of vessels of the pancreas as the cause. C. H. Mayo reported a case of paroxysmal hypertension in which the blood pressure was reduced to normal by removing a tumor which possibly originated in the sympathetic nervous system or in the suprarenal gland. Goldzieher and Molnár were able to demonstrate an increased amount of epinephrine in suprarenal glands from cases of hypertension. As recently as 1928, Goldzieher and Sherman demonstrated hypertrophy of the musculature of the veins in cases of hypertension and concluded, "Our results add new and weighty evidence to the theory which links hypertension and allied diseases with functional disturbances of the suprarenal glands." These observations and opinions suggest the constant

but increased liberation of epinephrine as a cause of hypertension. Such a condition has no experimental foundation, for, according to Markowitz, "In the experimental animal sufficient epinephrine to cause hypertension is enough to raise the blood sugar to an extreme diabetic level, dilate the pupils, paralyze intestinal and gastric movement and cause erection of hair along the neck and tail." Obviously these conditions do not exist in the human being with hypertension. Cannon and Lyman have further shown that small amounts of epinephrine injected into the cat cause a fall in blood pressure, a result which they explained on the basis of the state of muscle "relaxed when tonically shortened, contraction when relaxed." Janeway, in 1913, carried out numerous pharmacologic experiments with the blood of patients with essential hypertension. He concluded that the hypothesis that hyperepinephrinemia is a cause of hypertension was not supported by his results and characterized such a theory as a "beautiful dream." Ingier and Schmorl were unsuccessful in an attempt to demonstrate increased amounts of epinephrine in the suprarenal glands of individuals with hypertension. The technic described by Schur and Wiesel for demonstrating epinephrine in the blood has not withstood criticism. Recently Mosenthal has reviewed the evidence of hyperepinephrinemia as a cause of hypertension. He said "This idea has been categorically affirmed and denied by any number of observers, but definite proof of an excess activity of the suprarenal gland has not been furnished. The very presence of epi-

nephine in the blood, thus far, has not been demonstrated and the successful quantitative estimation of this substance has not been accomplished." The theory of hyperepinephrinemia as a cause of hypertension is at present subject to discussion. The rôle of epinephrine cannot be dismissed, however, without consideration of the effects of countless episodes of liberation of epinephrine over a period of years. The vasopressor effects of subcutaneously injected epinephrine are as short as two minutes. Markowitz has advanced evidence that epinephrine is destroyed in the walls of the blood vessels, an observation which agrees well with the known effects of repeated injections of epinephrine on the structure of blood vessels. Is it not possible that there is present a condition of localized activity of the sympathetic nerve supply to the suprarenal gland\* which releases numerous spurts of epinephrine over a period of years? As a result of the destruction of epinephrine in the walls of the vessels and overwork due to the greatly increased activity of vasoconstriction and vasodilation, may not anatomic changes occur in the systemic arteries? And may not hypertension be a direct result of these changes?

*Increased activity of the sympathetic nervous system.* The extremely close anatomic and physiologic connection between the sympathetic nervous system and the suprarenal gland has been emphasized. The same physiologic association between the general arterial system and the sympathetic nervous

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\*Such a condition of localized sympathetic hyperactivity is present in Raynaud's disease

system is well known. Stated simply, stimulation of the sympathetic system causes increased blood pressure by virtue of widespread vasoconstriction, and the same stimulus simultaneously causes impulses to be transmitted probably to the muscular walls of the veins of the suprarenal gland and probably causing them to contract. Hypertrophy of the muscles of these veins in all probability indicates increased functional activity, which occurs as a result of sympathetic overactivity. Changes in the musculature of the veins might then be an index to changes in the muscular coats of the arteries of the general systemic circulation, since both changes probably are of the same origin, that is, sympathetic overactivity. This opinion has some physiologic and clinical confirmation. Cannon showed increased liberation of epinephrine in the experimental animal under conditions of fear, asphyxia and pain. This is brought about by sympathetic activity, probably generalized, since Stewart and Rogoff have shown that the liberation of epinephrine is entirely controlled by the abdominal sympathetics. It seems likely that the same conditions as those induced under experimental circumstances are present in many human beings. In this modern age, with the greatly multiplied difficulties of living and adaptation to environment, there are numerous daily episodes of sympathetic stimulation as a result of emotional changes. This hypertrophy of the muscles of the veins of the suprarenal gland, as well as that of the systemic arteries, may be simply an expression of heightened susceptibility to external stimuli in individuals subject to hypertension. This

muscular hypertrophy may mean that the sympathetic nervous system is worked twice as hard in patients with elevated blood pressure and that the musculature has become twice as great in all vascular structures supplied by sympathetic nerves. Numerous observations on individuals in whom high blood pressure has been developing at the time of the observations have shown that there is an early stage of unknown duration, probably of many years, during which the blood pressure will descend to normal or nearly to normal under proper conditions of rest. This is the "functional" stage of hypertension. Later this condition does not obtain, the blood pressure is more firmly fixed at a high level, of which Elliott<sup>14</sup> has said, "It pursues its life history undeviatingly." Is this not the sequence of events (1) numerous stimuli to the sympathetic nervous system of a hypersusceptible individual, with vasoconstriction and a brief increase in blood pressure in response to each stimulus (functional hypertention), (2) hypertrophy of the musculature of all vascular structures supplied by the sympathetic nervous system as a result of these countless episodes of constriction and relaxation, and (3) fixed hypertension as a result of this hypertrophy? Elliott<sup>14</sup> has supported this view of widespread vascular overwork as brought out in the first of the sequence of events just suggested. "May it not be as good a surmise as any other that essential arterial hypertension is in its inception a vascular neurosis, that certain individuals possessing certain susceptibilities in their vascular responses transmitted by inheritance pass into a state

of vasomotor susceptibility as middle life approaches?"

If this theory of the neurogenic origin is tenable, the hypertrophy of the musculature of the veins could be explained as a direct result of increased activity of the general sympathetic nervous system. Certainly venous hypertension is not a factor, for the systemic intravenous blood pressure is not increased in cases of hypertension until the myocardium begins to fail. It seems justifiable to conclude that the pressure within the suprarenal veins is of similar value to that in the general venous circulation. The short time between the occurrence of failing myocardium and the demise of the patient, with the fact that the intravenous pressure never becomes great, would seem to exclude increased intravenous pressure as the cause of muscular hypertrophy in the suprarenal gland. Here is an interesting condition: on the one hand is increased intraarterial pressure (hypertension) with muscular hypertrophy in the arterial walls, on the other hand, normal blood pressure within the veins, and yet muscular hypertrophy of the veins. If the muscular changes in the systemic arteries and the suprarenal veins have the same origin (overwork), this is evidence that the hypertrophy of the arterial walls precedes or occurs concomitantly and does not follow the increased arterial tension, since there is no hypertension within the veins where similar muscular hypertrophy is present. Does this not indicate that we must hold with reservation the view that arterial muscular hypertrophy occurs as a result of hypertension? It seems more probable that the muscular changes are

cause and not effect of fixed hypertension.

*Reaction to noxious substances in the blood stream.* I have shown previously the shortcomings of the theory of constant hyperepinephrinemia as a cause of hypertension and I believe with Janeway that it is a "beautiful dream." The hypothesis of numerous episodes of liberation of epinephrine must be entertained with reservation. The theory of sympathetic overactivity as reaction to strain seems applicable in a large group of cases, but it fails to explain hypertension in children and in those phlegmatic individuals who apparently are free from abnormal responses to emotional stimuli. It may be reasonable in these instances to believe that there is widespread vascular hypertrophy, due to the effect of substances circulating in the blood stream, and that they produce their insidious effects on the venous and arterial walls, in a manner completely divorced from the emotional reaction of the patient. Is it not probable that hypertension is the physiologic answer to these changes in the walls of the vessels? This conception of the mechanism must rest on the findings of comparable changes in all other vascular structures with musculature. Unfortunately this information is not available. I found some evidence against it in my study as only the veins of intermediate size of the suprarenal glands participated in the process of muscular hypertrophy. It is difficult to understand why the other veins would be missed in a process due to a circulating toxic substance. Further study is needed. Comparatively too much attention has been given the study of

the small arteries of the systemic circulation, and far too little to veins. Particularly too little attention has been paid to the vessels of the pulmonary circulation where the nature of these changes is not complicated by increased blood pressure within the lumens. The study of the veins of the suprarenal gland avoids the factor of increased intravascular pressure, but the profuse supply of sympathetic fibers adds confusion. The pulmonary circulation should furnish excellent material for study, as here the intra-arterial pressure is increased little or none and vasomotor fibers are entirely or almost entirely absent. I hope to make such a study the basis of a future report.

#### CONCLUSIONS

1 Veins of the suprarenal gland, the individual areas of the lumens of which in cross sections are between

199 and 300 sq mm have, in cases of hypertension, a ratio of muscle to lumen twice as great as that in cases of normal blood pressure. Theoretically, this hypertrophy indicates the following (1) increased function of the suprarenal glands, (2) overactivity of the sympathetic nervous system, or (3) the effect of noxious substances in the blood stream.

2 The total area of the lumens of all veins, as defined in the paper, is greater in cases of hypertension than in cases of normal blood pressure. This shows that there is a higher degree of vascularization in the former which probably indicates a higher level of functional activity.

3 These observations are distinct evidence of a close relationship between increased functional activity of the suprarenal glands and hypertension.

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## Relation of Syphilis and Yaws\*

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**I**T is doubtful if any other disease has influenced more materially the destinies of the human race than has syphilis. No other human disease punishes ignorance so unerringly and unmercifully as does this one, for it is the only human disease which is commonly carried over from parent to child congenitally.

It is certain that for thousands of years mankind has been aware of the fact that this disease was often transmitted by sexual intercourse and it was the stigma of shame, attached to this fact which made him try to suppress all notice of the disease. For centuries since the renaissance which brought into the open truths of all kinds, facts about this disease have been suppressed and attempts have been made by the learned, who should have known better, to place the origin of syphilis to the credit of any other race of people than that to which the particular wise man who was doing the writing about it, belonged. When Columbus discovered America, the wise ones of the old world saw their chance to escape from the stigma in a body, so they placed the disgrace upon the

Carib Indians with whom he first made contact and the Great Discoverer, has ever since, been credited with having introduced syphilis into Europe upon his return there from his first voyage to Hispaniola. The fallacy of this has been pointed out by such masters in medicine as August Hirsch, Sir Wm Osler, Karl Sudhoff, and many others so that it is difficult to understand why any one at this time should subscribe to it. This would not be mentioned except to drive home the lesson, that we of 1929 who are so bold and frank in writing popularly concerning other sex matters are still sulking in the dark when it comes to giving out facts about syphilis in the public prints and we physicians are still clinging to the mediaeval folly. In a personal communication Dr Judson Daland told me recently that "the word 'syphilis' never appeared in English in the newspaper until about ten or fifteen years ago, and almost never appears in any magazine or newspaper today, although Edward Bok used the term in the *Ladies Home Journal* when he printed articles on the evils of venereal diseases."

It is paradoxical that our young people should know so much about sex psychology and Freudianism and so little about the facts of syphilis, a dis-

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\*Lecture and lantern demonstration given to the class in tropical diseases at Georgetown University Medical School, May 3, 1929



ease peculiar to the human species which has influenced so materially the welfare of man since first he made his appearance upon the earth

In describing what we mean by Yaws of Frambaesia, we will first give three definitions of the term in order that you may better understand. The first is that of Sauvages who briefly described it in 1768 and was, I believe, the first author to use the term "frambaesia" as a synonym for it. His work "Nosologia Methodica" is remarkable for its accurate description of diseases of every type. Nosologia may be said to sum up the medical knowledge of that day very accurately. Those of my hearers who have ever attempted to get an exact picture of the best knowledge obtainable upon any subject or specialty for any generation of the past, will understand what I mean when I say that Sauvages' work acts as a "point of departure" for the medical knowledge of 1750, just as that of Sydenham did for 1650 and that of August Hirsch did for the period 1850 to 1880. The following is a translation of Sauvages' Latin definition of Yaws. "Frambaesia, Yaw of the People of Guinea. Epian or Pian of the Americans, is a contagious disease endemic in Guinea and in the Americas *sometimes congenita* as shown by Father Labat\* with the Caribs, the principal symptom of which is the frequent eruption of mushroom-like growths with the color and shape of the raspberry whence the African name yaw, because it sounds like frambaesia to these symp-

toms are added eating ulcers, exostoses, caries, ankyloses and emaciation."

The second definition is that of the 9th Edition of the popular work of Manson-Bahr on Tropical Diseases just now off the press. "Yaws is a contagious inoculable disease, characterized by an indefinite incubation period, and followed usually by fever, by rheumatic-like pains, and by the appearance of papules which generally develop into a fungating, encrusted, granulomatous eruption. Running a chronic course, it is mostly protective against a second attack. The disease is caused by *Treponema pertenue*, and is controlled by salvarsan and certain bismuth salts."

The third conception is one which the speaker has committed to words, but this view regarding Yaws has been held for several hundred years and so taught by such great physicians as Thomas Sydenham and Jonathan Hutchinson. Here it is "Yaws is epidemic non-Venereal syphilis transmitted innocently amongst primitive peoples and under stone-age conditions of personal hygiene constitutes one of the exanthemata of childhood. It is then called yaws, frambaesia, pian, bubas and so on variously according to the race and language of those affected."

With the lantern we will show you examples of most types of the so-called yaws and will in many instances show parallel conditions in "orthodox Caucasian syphilis." From the last definition you will at once infer that yaws is a disease of the unwashed and ignorant. It is not wholly a disease of the dark-skinned races of man, as syphilis of the innocent has often been

\*Jean Baptiste Labat 1663-1738 1693-1705 in French colonies. *Nouveaux Voyages aux îles d l'Amerique* 1721

described in epidemic form for primitive whites. In the present state of civilization we find, however, that those primitive conditions which foster yaws are found mostly in the tropics and amongst the dark-skinned and the dirty. It is the most important of present day diseases which are confined rather strictly to the tropics.

If this definition is correct, the reverse of it should be demonstrable, and that we believe is capable of proof beyond question. To state this reverse proposition categorically, we will say that treatment, civilized clothing, shoes and habits change epidemic syphilis to venereal syphilis or "civilization syphilis" yaws. It makes an innocently acquired disease come to be a venereally acquired one.

The paradox of an actively contagious condition disappearing from certain islands and countries while maintaining its full reign in nearby islands or adjacent countries in close communication with the first, finds its only logical and satisfactory explanation in the above assumption. In Haiti syphilis is the city disease, yaws in its florid state is confined mostly to country districts. Of course, I do not mean to say that yaws is *never* venereally acquired. Doubtless a father or mother often acquires venereal syphilis and when the infective mouth or eruptive lesions are full-blown, the children of the household acquire "Yaws" innocently from this first case. No treatment being administered to any of them the whole infected family tails off into latent or tertiary syphilis, gangosa, goundou or juxta-articular nodes and no man knoweth "whence it cometh and whither it goeth." Verily

the ways of the *Treponema* are dark and devious, its manifestations protean and serious.

African slavery began for the New World in 1517 when Bartholome de Las Casas, afterwards bishop of Chiapa (1544) intervened at the court of Spain on behalf of the oppressed Indians of Haiti. He advised Charles V to permit each Spanish resident of the New World Colonies to import twelve African slaves. This first legalized slavery in America but a few African slaves had been imported into Haiti as early as 1502. In order to understand the speaker's explanation of Yaws and its wide prevalence present and past, in the West Indies it is essential to keep in mind the above historic facts, as well as the following. The Portuguese first began to explore the west coast of Africa as early as 1442. This was 55 years before Vasco de Gama rounded the Cape of Good Hope (the date was November 20-22, 1497) and fifty years before Columbus discovered the New World. Because of these West African discoveries the Portuguese made agreements with other contemporary Governments which gave them control of the slave traffic from West Africa for many years. During the 300 years following 1520 many millions of slaves were imported into the Americas from Africa. It is our belief that the Portuguese infected the "Slave-bearing" fringe of Africa with their venereal type of syphilis and that the 75 years of their contact with this coast through the slave trade before they began sending slaves to America was sufficient to give the negroes Portuguese syphilis. The negroes interpreted the white-man's syphilis in

terms of yaws and when the West Indian slave trade began, passed it back to him as such. This type we know was brought over in the slave ships from the earliest history of this deplorable traffic. Oviedo writing as early as 1529 assures us that what we now know as Yaws was present in Haiti at that time and that it was the same disease as in Europe was known as the French disease, the Neapolitan disease, etc. He remarks that in Europe it was known to be a disease of prostitutes and the lowest class of society.

Thomas Sydenham, known as the British Hippocrates who lived between 1624 and 1689, wrote about this disease and he interprets it almost exactly as did Sauvages 100 years later. He describes it thus: "But to me it rather seems to have taken its rise from some nation of the Blacks upon the borders of Guinea for I have been informed by several of our countrymen of great veracity, who lived in the Caribbee islands, that the slaves which are newly from Guinea, even before they land, and likewise those that live there, are afflicted with this disease, without having known an infected woman, so that it frequently seizes whole families, both men, women and children. And, as far as I can learn, this disease, which so frequently attacks these miserable people, does not at all differ from that we call the venereal disease, with respect to the symptoms, viz, the pains, ulcers, etc., allowing for the diversity of climates; tho' it goes under a very different name, for they entitle it the Yaws. Nor does their method of cure differ from ours, for in both cases a salivation raised by

quicksilver carries off the disease, notwithstanding what we say here of the excellent virtue of guaiacum and sarsaparilla in those places where they grow, which is judged to be nearly lost in their long passage to us."

In his accurate observations of the findings in "Parangi" which is the name for Yaws in Ceylon, Sir Aldo Castellani in the summary to his paper reporting spirochaetes in this disease uses the following words, "In 7 of 11 cases of Parangi spirochaetes have been found. Of these spirochaetes there is an extremely delicate variety, which in my opinion, is absolutely identical (sic) with the *Spirochaete pallida* (sic) of Schaudinn. If my hypothesis should be proved to be wrong, a proper name for the organism might be *S. pallidula*."

This was only a few weeks after Schaudinn and his co-workers had described *Treponema pallidum* and correspondence with this investigator developed the fact that Schaudinn's organism and that discovered by Castellani were indistinguishable morphologically. I might add that up to May 3, 1929, they are still indistinguishable not only morphologically but by any other means known to science.

It is impossible within a reasonable time to discuss each point of this question. But suffice it to say that evidence is at hand which would convince the open-minded investigator that Yaws is just syphilis which is operating under slightly different conditions of transfer from individual to individual. The identity can be proven as far as it is possible to prove anything in medicine by tests and studies old and new, arranged under the fol-

lowing heads, any one of which might occupy from a half minute to a half day depending upon the state of "openness" of the particular mind to accept facts. This statement presupposes that the individual to be convinced knows a reasonable amount about the different aspects of syphilis. These headings are (1) Etiology (2) Immunology (3) Clinical Course (4) Epidemiology (5) Pathology (gross and microscopic) (6) Prophylaxis (7) Treatment (8) History.

We may best define the attitude of those who contend that Yaws is anything else than syphilis in these words: They have taken a few symptoms of the protean disease we know as syphilis and define this collection of symptoms under the name of Yaws. All those cases of the larger symptomatology which do not come within this small group they call syphilis.

We may draw a parallel from what

obtains in plague. It is just as if we should say that flea-borne bubonic plague were the only real plague and that the droplet-borne pneumonic plague is not plague at all because it is generally communicated in a different way.

To those irreconcilables we recommend an unbiased study of the isolated population of Guam. This island has been in frequent communication with the white man ever since Magellan discovered it in 1520, that is to say for 409 years. A study of this population in relation to the infection under consideration will make unnecessary any animal experimentation to determine the identity of yaws and syphilis. The answer is given by correct reasoning upon the facts observed and recorded for this unintentional but very definite human experiment. In other words the answer is a matter of logic and not of "highbrow science."

## Editorials

### OUR CONFUSED CONCEPTIONS OF CHRONIC ARTHRITIS

As pointed out by J. Alison Glover in his report to the British Ministry of Health, chronic arthritis is no new disease, being equally as prevalent in the prehistoric dwellers of Nubia and Upper Egypt as in the Saxon forefathers of the Heptarchy. It occurs in the lower animals as frequently as in man. Accurate observations upon gout are found in the Hippocratic writings, and the 29th aphorism, Book VI, is as true today of the women of England as of the Greek women of the Archipelago in the Fifth Century, B. C. In the Third Century, B. C., Erasistratus employed modern hydrological methods, graduated exercise, diet and vapour baths in the treatment of joint affections. The following centuries contain little or no reference to the disease, and it was not until the time of Sydenham that chronic rheumatism of a form, incurable and lasting as long as life itself, was first described in medical literature. Sauvage, in his "Nosologica Methodica" (1763) divided gout into fourteen forms and rheumatism into ten. His *arthritis rheumatica*, or *goutte rhumatismale*, is most probably identical with the rheumatoid arthritis of the present day. To Sauvage's attempts at classification of arthritic conditions we probably owe much of the present day confusion attending chron-

ic arthritis. In 1795, Cullen made the first attempt to simplify this elaborate classification by recognizing only acute and chronic forms. Landre-Beurais in 1800 differentiated the "*goutte rhumatismale*" of Sauvage under the term of "*goutte asthenique primitive*". In 1829, Gruveilhier made the first definite differentiation of *osteoarthritis* as an individual entity under the designation of "*chronic rheumatic arthritis*". Adams, in 1831, applied the term "*malum coxae senilis*" to the monarticular form involving the hip joint. Scudamore had as early as 1827 emphasized the importance of the inflammatory changes in the periarticular connective tissues, to which Watson in 1843 again directed attention. Bright and Addison gave in 1839 their sanction to the use of the term "*rheumatic gout*" for chronic arthritis. Fuller (1852) divided rheumatic diseases into three chief divisions: *acute rheumatism* (*rheumatic fever*), *muscular rheumatism* (including sciatica and brachial neuritis), and *rheumatic gout* (including what is now termed rheumatoid arthritis and osteoarthritis). Garrod (1858) used the term "*rheumatoid arthritis*" to cover all forms of chronic arthritis save gout, on the assumption that what we now call rheumatoid arthritis and osteoarthritis are but different aspects of the same disease. Charcot agreed with Garrod in this view. The term "*arthritis deformans*" was introduced in

1860 by Virchow. Since that time confusion has reigned in the use of the three terms—rheumatoid arthritis, osteoarthritis and arthritis deformans, and this confusion of conception of chronic arthritis still holds in the medical literature of the day. The American Official Nomenclature makes rheumatoid arthritis a synonym for arthritis deformans. Hoffa and Wollenberg, in their work on "Arthritis Deformans," Stuttgart, 1908, take the exact opposite of this standpoint, and consider arthritis deformans a synonym of osteoarthritis, sharply distinguishing it from rheumatoid arthritis. An examination of the current standard textbooks shows the same confusion of usage. According to different authorities we may take our choice of views, as follows—arthritis deformans includes rheumatoid arthritis and osteoarthritis as different forms of the same disease (McCrae), rheumatoid arthritis includes a periarticular form and osteoarthritis (Taylor, Carter and Gibson), osteoarthritis includes all the chronic joint diseases (International List), arthritis deformans is a synonym for rheumatoid arthritis and quite distinct from osteoarthritis (American Official Nomenclature), arthritis deformans is a synonym for osteoarthritis and quite distinct from rheumatoid arthritis (Hoffa), rheumatoid arthritis and osteoarthritis are entirely separate and distinct diseases (Hoffa, Hale White, Llewellyn Jones, and Garrod), or all the terms, arthritis deformans, rheumatoid arthritis and osteoarthritis are synonyms and indistinguishable (Encyclopedia Britannica). This last-named usage is probably the most common

among English and American medical men of today; but the great variations in usage and standpoint make a serious situation, for one worker in the line of these diseases can never be sure that another in his own country or in a foreign country is using any one of these terms in the same sense that he is using it. Consequently the etiological and pathological basis of classification becomes hopelessly confused. Nothing is left for the individual observer but to put forth a new classification of his own. This has only served to increase the confusion, no one of the more recent classifications (Coates, Herbert, Strangeways, Fisher, etc.), based in part upon pathology and etiology, has helped to clear up this confusion. They have only served to emphasize the fact that a scientific classification of the many forms of chronic arthritis is not today possible, because of our ignorance concerning their etiology, pathogenesis and pathology. In attempting to clear up the situation, and to form a practical basis for the consideration of chronic arthritis diseases, the British Ministry of Health adopted in 1922 the following classification, to which it adheres in the present Report. This divides chronic arthritis into four groups: *Rheumatoid Arthritis* (including Infective Periarthritis), *Osteoarthritis* (including *Malum Coxae Senilis*), *Gout* and *Unclassifiable Chronic Joint Changes*. Rheumatoid arthritis usually begins with an acute attack of fever of considerable length, many smaller joints are usually affected, especially the 1st and 2nd phalangeal joints, spindle-shaped joints, and often involving the temporo-maxillary joint,

the changes are chiefly periarticular often accompanied by much fibrositis, the lesions are often bilaterally symmetrical, nutrition of patient is invariably bad, patients are usually females. The bone and joint cartilage usually escape obvious change in the first stage of the disease. The radiograph often shows little or no bony change. In the more chronic stages of the disease the formation of chondro-osteophytes occasionally produces lipping, but to a lesser degree and at a later stage than in osteoarthritis. All of the varieties of rheumatoid arthritis are at least three times more frequent in women than in men. The patients show a definite constitutional peculiarity, being chiefly of the asthenic, slender build, similar to that associated with tuberculosis. They usually show stigmata of a true toxemia in the form of a low continued fever, cold clammy hands and feet, inactive skin, pale bad complexion, poor appetite, and lowered general nutrition. The disease often begins with an initial attack of fever, which may closely simulate an attack of acute rheumatism, although the absence of any real reaction to sodium salicylate and the absence of the flitting from joint to joint and cardiac complications so characteristic of acute rheumatic fever, may help in the differential diagnosis, yet so close is the resemblance that the disease is often at first diagnosed and treated as acute rheumatism, the real diagnosis does not become apparent until the fever subsides. Then the patient finds that the joint inflammation persists instead of clearing up, her muscles waste, and pain, swelling and deformity remain. All forms of rheumatoid arthritis usu-

ally begin, more or less symmetrically, in the smaller joints, especially the first and second joints of the fingers, and, by the swelling of the ligaments and the surrounding fibrous tissue, the finger-joints assume a characteristic spindle shape. The early involvement of the temporomaxillary joint is very characteristic, so much so that Herbert considers its presence, together with pain, stiffness and grating in the back of the neck, the "jaw-neck syndrome," as a basic test for rheumatoid arthritis. The larger joints become involved later, and at first there is little deformity, except for the spindle-shaped swelling of the fingers and other joints. Atrophy of the muscles takes place early, and is very noticeable, later, muscular spasm leads to deformity of characteristic type. The hands assume a position of palmar flexion with ulnar deviation. Many varieties of rheumatoid arthritis have been described by various authorities. One of these, a peculiarly acute and intractable form occurring in young women deserves especial mention. In this form the initial attack is usually severe and the resemblance to acute rheumatic fever especially close. Little or nothing is known of its etiology, a recognizable focus of infection is rarely seen associated with it. It usually ends in the pathological form known as atrophic arthritis. Some American authorities (Goldthwaite) term rheumatoid arthritis "atrophic arthritis" in contrast to hypertrophic arthritis, but most English writers reserve that term for the form in which there is a marked rarefaction of the bone (about 6 per cent). *Osteoarthritis* is usually afebrile.

rile, shows a gradual onset often at first confined to one large joint, fewer and larger joints are affected, especially knees and hips. There is grating, hiping, eburnation and formation of osteophytes. The lesions are often asymmetrical and the patient is usually well nourished. The first change in osteoarthritis is a degeneration of the articular cartilage, especially where the pressure of the opposing cartilage is greatest. the cartilage here undergoes a process known as fibrillation, which has been compared by French to the changes in the cataractous lens. Under the worn cartilage the bone becomes eburnated, dense and ivory-like, and at the outer edges of the joint, both cartilage and bone proliferate. For a comparatively long time the synovial membrane may be unaffected, but eventually that portion nearest the articular cartilage becomes villous. The proliferated bone and cartilage form first a "hipping," and eventually osteophytes. These may become detached as free bodies and yet continue to grow. It is peculiar to this disease that, at the same time, and in the same joint, there is going on at the same time both absorption and production of bone. The changes are slow, but gradually give rise to great deformity, very different from that due to rheumatoid arthritis. All the fibrous tissue about the joint may be ossified, or may soften and disappear, and the joint may even become dislocated. Clinically osteoarthritis shows usually an insidious onset, beginning with stiffness and creaking in one or more of the larger joints. It is much less symmetrical than rheumatoid arthritis. The general health and nutrition of the body are

much less affected than in rheumatoid arthritis, and the disease is found especially in stout, well-nourished people. In the monarticular form of the disease, one large joint only, one knee, one hip, or shoulder is grossly diseased, but in this form too, it is usually possible to detect signs in other joints on careful search. Slight fever sometimes accompanies an exacerbation in one joint, but the course of the disease is, as a rule, free from fever. The skin in this affection is of normal color, even ruddy and warm, reacting well to external change. Osteoarthritis is throughout its course much more of a local or joint disease than is rheumatoid arthritis, which is so clearly a general systemic disease. The erosion of cartilage and the thickening of the synovial membrane give rise to a creaking and grating characteristic of the disease, and a sudden "locking" type of pain in the joint is also characteristic. The knee is most frequently involved (35 per cent in males, 55 per cent in females). In women the osteoarthritis of the knees so often seen between the ages of 45-55 forms a large part of the so-called *climacteric* arthritis. Some writers hold that osteoarthritis is but a different manifestation of the same disease as rheumatoid arthritis, others that it is but an end result of rheumatoid arthritis, while others claim that it is an entirely distinct disease. Fisher, who has made an extensive study of its pathology, says that it is not a disease *suu generis*, but is rather the series of physiological and pathological changes that ensue in a joint subjected to prolonged or oft-repeated injury, either mechanical or toxic, but of a moderate degree of



intensity The usual text book description is accepted for *acute gout* *Chronic gout* is regarded as a polyarthritis with a definite history of repeated attacks of acute gout or the presence of tophi Under *chronic joint changes unclassifiable* are grouped those chronic joint changes which cannot be allocated to any one of the three preceding forms About 15 per cent of all cases of chronic arthritis will have to be so relegated In the recent Ministry of Health Inquiry 13 per cent of the chronic arthritis cases were thus classified This British Report on Non-Specific Chronic Arthritis should be of special interest to American readers, because of the apparent increase in the number of patients showing various forms of the affection presenting themselves in American clinics, and,

also, because of the growing importance of the physical therapy of these conditions in the joints It is essential that each case of arthritis be given a thorough examination and carefully differentiated diagnosis, before physical therapeutic measures are instituted What is urgently needed is more light upon the etiology, pathogenesis and pathology of joint affections in order to clear up the ambiguity attending their terminology There is a tendency for these cases to collect in certain institutions and sanatoria Wherever this is the case advantage should be taken of the situation in the provision of proper equipment for observation and diagnosis, as well as for the treatment, otherwise the latter tends to become too empirical

## Abstracts

*A Report on Chronic Arthritis With Special Reference to the Prevention of Treatment*. By J. Alison Glover O.B.E., M.D., M.R.C.P., D.P.H. (Reports on Public Health and Medical Subjects No. 52 Ministry of Health, London, 1928)

This is the third report submitted to the British Minister of Health concerning the public health and preventive aspects of the so-called "rheumatic diseases." The first, published in 1924, dealt especially with the incidence of rheumatic diseases in adult insured persons, the second report, published in 1917, dealt with acute rheumatism in children in its relation to heart disease. For presentation in an official report few subjects could be more involved than that of chronic arthritis, because of its confused nomenclature and our ignorance of the exact causes and real nature of this condition. Yet while its etiology is still obscure its treatment is entering a more hopeful phase, and even in the existing state of knowledge there is much that can be done to prevent, to alleviate, and even to cure chronic arthritis which is not being done. Non-specific arthritis is alone considered in this report, acute surgical arthritis, pneumococcal, scarlatinal, gonococcal, tuberculous, syphilitic, dysenteric, meningococcal, hemophilic arthritis and that due to injection of serum are excluded. Following the precedent of the previous report on Acute Rheumatism, the statements in the author's summary are not advanced as "conclusions" or as proved by the subject matter of the report. Our knowledge of the etiology and our experience as to the results of the treatment suggested are alike too limited and imperfect to permit of any "conclusions" in the strict sense. Nevertheless, his summary represents what, in the opinion of the writer, appears to be the present position. Chronic arthritis, while constituting a disease group that is inconspicuous

as a cause of death and almost absent from in-patient hospital statistics, is nevertheless one of the greatest factors in the production of suffering and invalidity. It costs the community immense loss in time and work, and causes a drain upon the National Health Insurance funds amounting to at least one-fourteenth of the total sum paid in sickness and disablement benefit. Chronic arthritis affects chiefly persons of middle and old age, and except in the case of gout, women more than men. Rheumatoid arthritis, however, usually has an earlier age of onset than the other forms of chronic arthritis, and begins more frequently between the ages of 20-30 than in any other age period. Its acute form often begins in girls under 20. The etiology of chronic arthritis is still imperfectly understood. It is probable that there are several important factors in its production. Of these factors, focal sepsis appears to be the chief, and there is definite evidence, more often than not, that it has played a leading rôle in the individual case, but diathesis, faulty metabolism, trauma, occupational stress, mental stress, senile change, and derangement of endocrinal balance seem all to be important factors. Unfortunately some of these terms are fully as ill-defined as is chronic arthritis, so that there is danger lest the explanation may seem to explain the unknown in terms of the unknown. In any case, it seems clear that chronic arthritis is a pathological condition which, like food poisoning or bronchitis, can be produced by a variety of agents or causes. This uncertain etiology gives rise to great difficulty in the classification of the several diseases in the group, and is the main cause of the wide variation in the use of the terminology. No satisfactory classification can be arrived at until more is known as to the etiology, but, apart from gout, two broad groups are distinguishable—namely, rheumatoid arthritis and osteoarthritis. The climacteric arthritis of

women at the menopause is considered by some sufficiently clear-cut to deserve a class to itself. Many systems of further subdivision have been devised, but none has received general consent. These fundamental uncertainties can only be cleared up by continuous and intensive study, from every viewpoint, of large numbers of cases of patients in the early stages of the disease. To this end an organization, which includes full facilities for assembling together sufficient patients, and for thorough diagnosis, careful records, complete equipment for early and adequate treatment, and an effective system of following up, seems essential. It would appear that to achieve such an organization the provision of one or more special "units" is necessary. A proportion of cases of chronic arthritis (amounting perhaps to 10 or 15 per cent, and including many of those acute cases which occur in comparatively young female patients) are exceedingly intractable to treatment of any kind. These cases have produced an impression, which still survives in many quarters, both professional and lay, that chronic arthritis is an incurable disease. On the other hand, whilst no specific remedy is known, it would seem that a much larger proportion, perhaps one-third of all cases, can be cured, and more than another third relieved to a greater or less extent by early, appropriate and skilful treatment. Far from chronic arthritis being incurable, there are few disease groups in which early and proper treatment is more necessary or more effective. The more important sites of focal infection associated with chronic arthritis are those connected with the teeth, tonsils, the accessory sinuses, the genito-urinary system and the bowel, the first two mentioned being by far the most frequent. The organism most frequently found in focal sepsis associated with chronic arthritis is the non-hemolytic streptococcus *veridans*. If there be a recognizable focus of infection in a patient suffering with chronic arthritis, the first indication of treatment is to remove it if it be removable, if not removable to drain or treat it. To undertake other treatment in the presence of an unremoved or untreated focus can only be correct treatment in certain very exceptional cases. The

removal of the focus must be conducted with due regard to the age, resistance, and general condition of the patient, the possibility of the procedure being made worse temporarily by increasing absorption being borne in mind, as well as the risk of shock. Where extraction of teeth is necessary the utmost care in clinical and radiographical examination must be taken to insure, on the one hand, that only thoroughly incriminated teeth are removed, and, on the other, that no septic root or diseased bone is left behind. The question of focal sepsis having been thoroughly explored, treatment of many other kinds has to be considered, whether it be immunological, dietetic, physical or surgical, or by means of drugs. Any of these treatments, if correctly applied, may be of value in suitable cases, but in practice a combined treatment is generally used. To achieve success requires long experience with the subtleties of the syndrome and real familiarity with the intricate niceties of the treatment used. It demands also a masterful yet persuasive personality and great patience in the physician. Each case must be treated individually and on its own merits. Immunological treatment is of value in certain cases—specific treatment with autogenous vaccines, particularly in comparatively early cases, and non-specific protein therapy either in early cases where a focus cannot be determined or in older cases apparently at a standstill. Some authorities use non-specific protein therapy by preference in all cases in which immunological methods are indicated. Dietetic treatment, particularly in the shape of low caloric feeding, is useful with the more robust patients, especially those with osteoarthritis and climacteric arthritis. Many patients with rheumatoid arthritis, on the other hand, require a generous diet, rich in vitamins B and D. Thyroid treatment is of service in certain cases. Physical treatment is of great value at some stage in almost every type of chronic arthritis. No scheme of treatment for chronic arthritis can be considered complete unless a large range of physical methods under skilled direction is provided. There is an urgent and rapidly increasing demand for physical treatment, which demand already far ex-

ceeds the provision and which may increase very rapidly in the future as the education of the public in the value of such treatment increases. The most important forms of physical treatment for chronic arthritis are electrical treatment, including diathermy, radiant heat and ionization massage and exercises, and the various forms of hydrological treatment. Hydrological treatment, if not an essential part of the physical treatment of chronic arthritis, is an invaluable adjunct. It is important for the resorption of inflammatory products, for the relief of pain for the restoration of lost motion in the joints and lost reaction in the skin, and for the reeducation of wasted muscle. Hydrological treatment has its fairest hope of success when given as spa treatment, i.e. when the patient can devote his whole time to the treatment in favorable surroundings, with the advantages of change of air and regimen, and in some cases the additional advantages of the specific therapeutic qualities of the natural waters of the spa. Many forms of hydrological treatment can however, also be given with great benefit to patients, using ordinary waters at hospitals other than spa hospitals and at out-patient clinics. Physical and hydrological treatment involve special experience, specially trained staff, and special equipment, and these can only be secured economically if the treatment, as far as out-patients are concerned, be given in centers suitably equipped to deal with large numbers of patients. Such physical treatment centers (including, of course, the special out-patient departments of certain general hospitals) should also be arranged to act as clearing houses, directing patients as to the form of treatment particularly suited to their special need and the place where it may be obtained. Some cases need the removal of a focus of infection, some the intensive study of an arthritis unit, others are suitable for treatment at a spa or spa hospital, whilst others would be greatly benefited by regular out-patient treatment at the center. These centers should be organized in closest liaison with the "arthritis unit" and with the spa hospitals, and should provide the continued supervision, observation and necessary after-care which should follow institutional treat-

ment. Such centers would be of the greatest service in many conditions other than arthritis, notably fractures and injuries, deformities, fibrositis and diseases of the nervous system. For the necessary research into the etiology and into the relative and real values of methods of treatment an "arthritis unit" housed either in a large wing of a general hospital, or in a separate institution, is required. This unit should be situated near, and work in closest cooperation with, either a university or a large teaching school of medicine, which would enable it to fulfill the purposes of research and observation as well as of treatment. Here patients would come at the earliest stages of their disease for thorough examination by modern methods, for diagnosis and for record, here the focus of infection would be sought, and, if possible, found and removed, here the necessary bacteriological, biochemical and radiographical work could be completed before the patient was passed on to the spa hospital or to the physical treatment center, or convalescent home, to complete his cure, here orthopedic surgery, or the fitting of the more elaborate appliances occasionally necessary in advanced cases, would be performed. In regard to preventive measures no directly prophylactic procedure can be urged, but many important indirect measures may be mentioned. Of these the recent development of dental benefit is probably one of the most important, following, as it does, the immense reduction of dental sepsis in children due to the school medical service. The prevention of dental caries is too large a subject to be discussed here, but the means available in the present state of our knowledge fall under four heads: (1) education of the people as a whole in the value of good teeth and the disadvantages of diseased teeth, (2) the supply of a proper diet adequate to promote the growth of perfectly formed and regular teeth, (3) instruction in the daily practice of oral hygiene, including the use of a detergent dietary, and (4) regular periodical dental inspection and treatment of the teeth. Pickerill advocates, in addition, that all meals should contain a fair proportion of salivary excitants, and, more important still, should both commence and end with some article of diet having

an acid reaction The attention to tonsillar sepsis in the school medical service also seems likely to diminish the incidence of acute rheumatism in children The increased attention to the question of lead solvency in water may be a factor in the reduction of gout, which seems to be in progress, and may perhaps be of service with certain forms of nephritis The importance of the prevention of dampness in the sites of dwellings and in the dwellings themselves, and the importance of the free circulation of air and of sunlight about dwellings is probably great in the prevention of most kinds of arthritis Dampness in a dwelling is an unmixed evil alike to the structure of the house and to the health of the inmates The provision of pithead and works baths, and the proper first aid treatment of minor sepsis, are perhaps only slightly less important in the prevention of arthritis than in the prevention of fibrositis Overeating

or drinking, bad at any time, become destructive as we approach middle life—the period of chronic arthritis Then there are important means of maintaining the muscular tone, and the skin reaction of the individual, as well as his resistance to disease Bathing, sun bathing, games, sports, exercises—particularly those in the open air—are of the utmost importance in counteracting the evil effects either of sedentary occupation, or the special stress of occupational trauma Then, too, are important the prophylactic effects of correct posture, and the prevention of postural and static deformities, scoliosis, flat feet and many another ill “We grow old because we stoop, rather than we stoop because we grow old,” says one distinguished authority on physiotherapy We must keep supple, “Not tied or manacled with joint or limb” Function is the important thing The disordered function is the disease

## Reviews

*How Ever, One Ought to Know* By  
OLIVER T. OSBORNE, M. A., M. D., F. A. C. P.  
311 pages — XIV Charles C. Thomas,  
Springfield, Illinois, and Baltimore, Mary-  
land, 1929. Bound in green cloth. Price  
\$2.50.

The object of this book is to present in simple language some of the truths concerning the wonderful mechanism of the human body and to outline some of the delicate physiologic processes which insure growth and maturity, and promote nutrition and health. To further the objective of "keeping well" nutrition, foods, exercise and general hygienic rules are discussed. The various infective causes of ill health are listed, and how they are acquired and the efficient measures of prevention are described. Chapters are devoted to the growth of children, to their mental and physical health and to their early school life. Some of the many accidents that occur to civilized people are discussed from the standpoint of the layman and his responsibility in giving first aid. The book is not intended to offer treatment for diseased conditions. Self-treatment is always of doubtful value and is frequently dangerous, often allowing a simple indisposition to develop into serious acute or chronic disease. The author sincerely hopes that the book will cause a better understanding of one's self and one's fellows, and that it will promote health and aid in preventing disease and its consequent unhappiness and even financial stress. The contents consists of seventeen chapters, as follows—Growth and Development, Functions of the Body, Nutrition, Foods, Diet, Promotion of Health, The Mouth, The Child, Some Statistics, Exercise, Infection, Prevention of Disease, Habits, Accidents, Poisons, The Skin and Nostrums and Quackery. The material in these chapters is well chosen and expressed in good, simple language. It is distinguished for its safe and sane common sense. The reviewer notes

with interest the author's views on the use of iodized salt and water for the general population, and wholly agrees with them. "Iodized salt is advertized. When these salts were first prepared they contained too much iodine and were not safe. Though containing less iodine at the present time, they still should not be used. One person eats much more salt than another, hence he would get much more iodine than one who ate but little salt. In other words, the dose of iodine in iodized salt can not be regulated. Iodized salt and iodized water supplies are not safe, as they may cause serious trouble with the thyroid gland. The prevention of goiter should be individual, and should be directed by a physician. It is not safe to iodize people by the wholesale or by city water supplies." With all of which we are heartily in accord. The writer shows a similar good common sense in his treatment of diet and nutrition. On the other hand he appears to be too much influenced by current fads of focal infection, especially as far as the teeth and tonsils are concerned. What scientific proof exists in the literature for the statement that "acute inflammation of the joints and acute disease of the heart most frequently start from the tonsils"? Surely such a flat statement as this cannot go unchallenged. The reviewer wishes that the author had shown the same conservatism of statement in this respect that he did in regard to iodized salt. On page 220, the reviewer notes the use of the expression "pusy inflammation," an example of incorrect spelling as well as of poor choice of terms. The same error is repeated on page 287. The author shows a curious one-sided view of the relative importance of habits. Under this chapter heading practically only two things are considered, Narcotic Drugs and Tobacco. Certainly much could have been said to the point with reference to alcoholism and various other habits of greater importance than these two. This book

contains much information of real value, but is very far from being the "complete health book" it is advertised to be. Notably among the important omissions is all reference to the reproductive function, with its various problems, light upon which the average human being needs most of all, and most earnestly seeks. Any book, pretending to be a health book in any sense of the word, which is as devoid of enlightenment upon this subject, as is this present volume, certainly fails of achievement. The venereal diseases are not even mentioned in the index. One has come to expect Health Books to be written by some propagandist or other of some especial fad or other. This book seems to be especially free from this taint, only a suspicion of which exists in the sections on coffee and tobacco. On the whole it is a safe book to put before the public which needs so much informing and instruction along health and disease lines. Yet the reviewer regrets that it could not have been made more complete, and written upon a broader view-point. The ideal book of health has yet to be written—probably never will be written—owing to the excessive fluidity and constant progression of the subject.

*Clinical Aspects of Venous Pressure*. Macmillan Medical Monographs. By J. A. E. EYSTER, B.Sc., M.D., Professor of Physiology, University of Wisconsin, Associate Physician, Wisconsin General Hospital, Madison, Wisconsin. 135 pages, 7 illustrations. The Macmillan Company, New York, 1929. Price in cloth, \$2.50.

While important advances have been made during the last two decades in the knowledge and clinical application of arterial blood determinations, the significance of venous pressure, on the other hand, has been greatly neglected. Although the latter does not appear to have the same degree of interest as the former in a number of more or less diverse clinical states, recent work has tended to emphasize its paramount importance in present or impending cardiac decompensation from any cause, or when there is reason to anticipate the possibility of this event during the course of several diseases. Venous pressure is the most direct indication that can be obtained clinically of the

extent to which the heart is moving its load of blood from the venous to the arterial side of the circulatory system, and it exhibits changes which precede the development of other signs and symptoms when the heart fails to do this to the normal degree. By far the greater part of the clinical situation in cardiac failure is due directly to venous engorgement, exhibited as passive congestion in various organs, and as exudates from serous membranes. As such engorgement occurs, the venous pressure rises, to fall again as the engorgement is reduced or disappears. Venous pressure may therefore be said to represent not only the primary factor that underlies the symptoms and functional pathology of cardiac failure, but to be also responsible in large part for the physical signs accompanying it, namely edema, congestion, cardiac dilatation and reduced urinary secretion. As the principal underlying factor in these conditions, and as the principal index of cardiac behavior, it is the most reliable and important single factor to know and to follow accurately when this clinical state develops, or when it is impending. Determination of venous pressure by the indirect method of vein compression is accurate, and can be readily and quickly carried out. It requires no more experience in order to secure confidence and accuracy than arterial pressure determinations. Although this method has been available and its importance more or less evident for a number of years, it has had by no means widespread clinical use in this country or abroad. It is hoped that the present book, written primarily for clinicians, and to stress the clinical application of venous pressure, will stimulate an interest which can only make for a better recognition, understanding and treatment of cardiac decompensation. Since an understanding of normal conditions must precede the interpretation of abnormal states, a brief review and presentation of the present conception of the cause and significance of venous pressure is given, followed by a discussion of the altered state that exists in cardiac decompensation. The conception of this condition which is presented has come in many of its details only recently through a more thorough understanding of cardiodynamics,

especially in its relation to venous pressure. The reviewer is wholly in accord with the theses of the author's preface as presented above. Venous pressure is as important clinically, if not more so, than is a consideration of arterial pressure, and the one-sided view of circulatory conditions prevailing in our clinics has always seemed inadequate and based upon a too narrow viewpoint. It is true that the majority of our clinical cardiologists practically disregard venous pressure as an important adjunct in the determination of cardiac compensation and decompensation, relying wholly upon arterial pressure and general cardiac phenomena. While recently the study of the capillary bed has been shown to throw additional light upon the circulatory state, there has been too great a neglect of the study of the venous pressure in the obtaining of the complete picture of the circulation as a whole. The material of this book is presented in eight chapters and an introduction. In Chapter I the mechanics of venous pressure in the normal and its relation to cardiac activity is discussed, in Chapter II cardiac decompensation, in Chapter III methods, in Chapter IV venous pressure range in the normal individual and the influence of various factors, in Chapter V venous pressure in cardiac decompensation, in Chapter VI venous pressure in conditions other than cardiac failure, while clinical cases are discussed in Chapter VII, and a general summary and bibliography complete Chapter VIII. The book is well written, in a clear, scientific style, and contains much recent clinical information relating to the circulation. It is a valuable contribution to the science of cardiology and performs a very important function in bringing to attention the much neglected field of venous pressure.

*Diseases of the Skin*. By RICHARD L. SUTTON, M.D., Sc.D., LL.D., F.R.S. (Edin.), Professor of Diseases of the Skin, University of Kansas School of Medicine, Assistant Surgeon, U.S. Navy, Retired, Dermatologist to the Santa Fe Hospital Association, Dermatologist to the Bell Memorial Hospital, the Swofford Home for Children, The Nettleton and Armour Homes for the Aged, and Visiting Der-

matologist to the Kansas City General Hospital. Seventh Edition. Revised and Enlarged. 1394 pages, 1237 illustrations and 11 colored plates. The C. V. Mosby Company, St. Louis, Missouri, 1928. Price in cloth, \$10.00.

That a seventh edition of this work should have been called for within two years of the publication of the sixth speaks sufficiently strongly for its popularity. At the time of the publication of the sixth edition it was thought that a new impression once in every three years would be sufficient to take care of all future needs, but the continued indulgent reception of the work, together with the accumulation of a large amount of new and valuable material has rendered this plan impracticable. Several recently discovered diseases have been introduced, the descriptions of some of the older ones rewritten, and the importance of others, such as certain of the occupational dermatoses, and those relating to allergy, emphasized. An attempt has been made to discuss intelligently the latest developments in cutaneous therapy, and to recommend those agents known to be reliable and practical. Much that is of theoretical interest only has been omitted, since a textbook is no place for the discussion of experimental medicine. Owing to the increase in size, the author has endeavored to get rid of all obsolete matter and to condense the new material as much as is consistent with clarity. In order to further economize space, a considerable number of valuable references have had to be confined wholly to footnotes, as otherwise the volume would have been so bulky and unwieldy as to impair seriously its usefulness. All of the changes that have been made in this edition have greatly improved it, and the work as it now stands is the most complete and up-to-date textbook on dermatology published in English, and the best illustrated of any published in any language. The author has an especial facility for seizing upon the most salient features of the various conditions described, and for giving these features an unusual clarity of presentation. Hence its great value clinically. The various personal touches add to its efficiency of presentation, as well as greatly increasing their interest. The book



is unusually free from diffuseness, in a subject so complicated as dermatologic conditions with their apparent overlapping and difficult clinical differentiation Dr Sutton has been singularly fortunate in presenting the essential entity of each affection. The ability to do this constitutes an especial art of the dermatologist who is also naturally a teacher. The great richness in illustration

constitutes another valuable feature of this book, and it is especially noteworthy that a large proportion of these are microscopical. Thus the relation between the clinical appearance and the pathologic changes underlying these is made clear. We heartily recommend this textbook as one of the most efficient and effective textbooks on dermatology that has yet appeared.

## College News Notes

### COMMITTEE ON NOMINATIONS FOR 1929-30

In accordance with the amended By-Laws of the College, President John H. Musser, on April 25, appointed the following Committee on Nominations for the year 1929-30: W. Blair Stewart, Chairman, Atlantic City, N. J., E. B. Bradley, Lexington, Ky., James S. McLester, Birmingham, Ala., J. H. Means, Boston, Mass., Charles F. Martin, Montreal, Que. The By-Laws provide "He (President) shall appoint within one month after induction to office a Nominating Committee of five, composed of two members of the Board of Regents, two members of the Board of Governors and one Fellow at large, whose duty it shall be to nominate candidates for the elective offices, Board of Regents and Board of Governors. The selection of the nominees for the Board of Governors shall be made after due consideration of suggestions of members from the respective states, provinces or districts which will be represented by the nominees, if elected. The list of nominees for President-elect and for the 1st, 2nd and 3rd Vice-Presidents shall be submitted to all the Masters and Fellows of the College at least one month before the Annual Meeting, and the election of all nominees shall be by the members of the College at its annual business meeting. This does not preclude nominations made from the floor at the annual meeting itself."

Dr. Leon Thayer Stem (Fellow), Chattanooga, has been elected President for 1930 of the Tennessee State Medical Association. From an editorial in the Journal of the Tennessee State Medical Association, it is stated that "Dr. Stem is one of the leading Internists of Chattanooga. He is a man of good judgment, has a high sense of justice, and has always shown an interest in upholding the traditions of medicine. In selecting its President for 1930, the

Tennessee State Medical Association has followed the spirit of our country, which selects its leaders and honors those whose ability and determination make for them a place of leadership."

Dr. Oliver T. Osborne (Fellow), New Haven, is the author of a new book entitled "What Everyone Ought to Know," published by Charles C. Thomas, Springfield, Illinois. The book is on health and how to preserve it.

At the 32nd Annual Session of The American Gastroenterological Association held at Atlantic City, New Jersey, May 6th-7th, Dr. Frank Smithies, Chicago, was elected President.

In the June, 1929, issue of *Annals of Internal Medicine*, page 1359 of the News Notes Section, reference was made to Dr. George R. Minot having resigned as head of the Medical Service of the C. P. Huntington Memorial Hospital during March, which by inference would be taken to be 1929. His resignation took place March 1, 1928.

Dr. George R. Minot (Fellow), Boston, addressed the Massachusetts Medical Society on June 12 on the subject, "Treatment of Anemia." He addressed the Maine State Medical Society at Poland Springs, Maine, June 18, on the same subject.

During Commencement week, Dr. Minot was elected an honorary member of the Harvard Chapter of the Phi Beta Kappa. He also received the Kober Medal of the Association of American Physicians on May 8, 1929.

Dr. P. P. McCain (Fellow), Sanatorium, N. C., was selected by a special Committee of the Moore County Medical Society for the award of the annual medal for 1928 for his paper on "The Diagnosis and Signifi-

cance of Juvenile Tuberculosis" The Committee's report states that they gave careful consideration to papers recommended by the sub-committees from each section This Committee grades each paper, taking into consideration original work and other regulations adopted by the House of Delegates

Dr Gerald B Webb (Fellow), Colorado Springs, as guest of honor at the Omaha meeting of the Nebraska State Medical Association, May 14-16, delivered an address entitled, "Early Diagnosis of Pulmonary Tuberculosis"

At the Tenth Annual Meeting of the Medical Staff of the Mt Sinai Hospital, of Chicago, Dr Maurice Lewison (Fellow) was elected permanent honorary President

Dr Allen K Krause (Fellow), for several years associated with the Johns Hopkins University Hospital, has accepted the Directorship of The Desert Sanatorium and Institute of Research, Tucson, Arizona While Dr Krause has already assumed many of the responsibilities of the post, he will probably not take up his resident duties until early fall Dr William Paul Holbrook (Fellow) is acting as Associate Director of The Desert Sanatorium and Institute of Research, and Dr Charles W Mills (Fellow) is Acting Medical Director

Dr William Fitch Cheney (Fellow), San Francisco, is President of the Commonwealth Club of California for 1929

At the 32nd annual meeting of The Washington Medical and Surgical Society held at Washington, D C, May 4th, Dr Frank Smithies, Chicago, was the guest of honor and delivered the Annual Address upon the subject, "Intestinal Protozoiasis as Clinically Manifested in the Temperate Zone" Dr Smithies was elected honorary member of the Society

Dr. Hans Lisser (Fellow), San Francisco, is Vice-President of the California Academy of Medicine, Councilor of the Association for the Study of Internal Secretions, Chairman of the Executive Committee of the

San Francisco County Medical Society, Associate Clinical Editor of *Endocrinology* and a Governor of the American College of Physicians

At the 32nd Annual Session of The American Gastro-Enterological Association, held at Atlantic City, N J, May 6-7, 1929, Dr Frank Smithies, Chicago, donated a fund with the object of the Association's securing annually a guest speaker of national prominence in research work The proceeds of the fund assure an honorarium to the invited guest of \$100.00 This annual address is to be known as "The Walter C Alvarez Lecture"

"Dr James M Anders (Master) received the honorary degree of Doctor of Laws from the Pennsylvania Military College on June 19, 1929, on the occasion of the Annual Commencement of that Institution"

The President-elect of the American Medical Association, elected at the Portland Session, Dr William Gerry Morgan, was born in Newport, N H, May 2, 1868 He received his A B degree from Dartmouth in 1890 and his M D degree from the University of Pennsylvania in 1893 After postgraduate work, he began practice in Southport, Conn, in 1894, and then removed to Washington, D C, in 1899 In Washington, Dr Morgan early made a place for himself in various medical and social activities He became professor of diseases of the digestive tract in Georgetown University and has held that position since 1904 He was chairman of the Advisory Draft Board in the district during the World War and also lieutenant in the Naval Reserve Corps Dr Morgan has held positions in many medical organizations, serving as chairman of the Executive Committee of the American College of Physicians, as president of the American Gastro-Enterological Association, as president of the Clinico-Pathological Society He is also a member of the American Therapeutic Association and of the New York Academy of Medicine In the American Medical Association, Dr Morgan was for several years a member of the House of Delegates

Dr L I Moorman (Fellow) Oklahoma City delivered an oration entitled 'Social Aspects of Tuberculosis' before the Thirty-seventh Annual Session Oklahoma City, May 20 1929

Dr F H McCrivy (Fellow) McAlester Okla addressed the General Session of the Oklahoma State Medical Association May 20 on 'Keep the Well Baby Well'

Dr Kenneth M Lanch (Fellow), Charleston S C was chosen president-elect of the American Society of Clinical Pathologists which met at Portland during the annual meeting of the American Medical Association

Dr David Riesman (Fellow), Philadelphia, Pa, addressed the Central Tri-State Medical Convention at Portsmouth Ohio, on May 16

Dr Ivell Cary Kinney (Fellow), San Diego Calif, was elected president of the California Medical Association during its meeting in San Diego on May 12

Dr Willard C Stoner (Fellow), Cleveland, attended the American Medical Association meeting at Portland, Ore where he discussed the "Chaos of Institutional Drug Therapy and Patient Management" before the section on Pharmacology and Therapeutics, after which he is touring the West, visiting hospital clinics and making a trip into Alaska

Dr Joseph H Barach (Fellow), Pittsburgh, Pa, was elected Medical Director of the Falk Clinic Falk Clinic is the outpatient department of the Medical Center, University of Pittsburgh Plans for the clinic building have been approved, construction to begin at once The clinic will have a working capacity of about 750 patients daily

Dr E Roland Snader Jr, (Fellow) is the author of an article "Hypothyroidism," which appeared in the March issue of the Hahnemannian Monthly

Dr Carl V Vischer (Fellow) of Philadelphia, was elected a Visiting Physician to St Luke's Hospital at a meeting of the staff on February 23, 1929

Dr Linn J Boyd (Fellow) of New York City is the author of an article, "Gastric Carcinoma" which appeared in the March issue of the Journal of the American Institute of Homeopathy

Dr Carl V Vischer (Fellow) of Philadelphia is author of an article, "Instructions for the Tuberculous Patient Relative to Prevention," which appeared in the May issue of the Medical Searchlight

The following Fellows of the American College of Physicians are members of the International Committee of the American Institute of Homeopathy which sailed from Montreal for Europe on June 27 Dr G Morris Golden Philadelphia, Dr Henry I Klopp, Allentown Pa, Dr Linn J Boyd, New York City The committee will meet with the British Homeopathic Medical Society in London with the French National Homeopathic Society in Paris and with the German National Homeopathic Organizations in Berlin and Stuttgart

Dr C Lydon Harrell (Associate), Norfolk Va was elected President of the Norfolk Medical Society on June 3 for the succeeding year This society has a membership of 178 physicians from Norfolk, Portsmouth and surrounding territory

Dr Samuel A Lowenberg (Fellow) of Philadelphia is author of a book "Diagnostic Methods and Interpretations in Internal Medicine" published by F A Davis Company, Philadelphia, Pa

Dr Karl V Vischer (Fellow) of Philadelphia was elected a Vice-President of the Alumni Association of Hahnemann Medical College, Philadelphia, at the annual meeting on June 6

Proceedings of the International Assembly of the Inter-State Post-Graduate Medical Association of North America, Atlanta,

Georgia, Session October 15, 19, 1928, was edited and published for the Association by Dr Edwin Henes, Jr., (Fellow) of Milwaukee, Wisconsin. The book contains essays by the following Fellows of the American College of Physicians, Dr Lewellys F Barker, Baltimore, Dr Walter A Bastedo, New York City, Dr A S Warthin, Ann Arbor, and Dr Harlow Brooks, New York City.

Dr Arthur C Morgan (Fellow) of Philadelphia and Dr Lewellys F Barker (Fellow) of Baltimore, Md., are members of the committee on the "Cost of Medical Care" whose chairman is Dr Ray Lyman Wilbur.

At the 41st Semi-Annual meeting of the Eleventh Councilor District Medical Association held at Huntington, Indiana, May 16th, Dr Frank Smithies, Chicago, was the guest of honor. Dr Smithies conducted a morning clinic at The Huntington County Hospital and in the afternoon addressed the society upon "A New Physiological Method for the Examination of Patients Affected with Intestinal Stasis."

#### RESOLUTIONS

Passed by the Council of the Chicago Roentgen Society June 24, 1929

WHEREAS, the storage and preservation of used x-ray films has recently become an economic and insurance problem and

WHEREAS, the reports of the roentgenologists responsible for the diagnoses are of decidedly more value and importance than the films, and

WHEREAS these reports are filed with, and become a part of the records of each case, making it unnecessary that large numbers and quantities of old and used x-ray films be preserved and retained for long periods of time, it is therefore

RESOLVED, by the Council of The Chicago Roentgen Society, acting officially for The Chicago Roentgen Society, that it is the sense and judgment of this Society, that it is not necessary to preserve any x-ray films for a longer period than two years after their exposure and that in all cases where there is no likelihood of legal proceedings—

such as ordinary clinical cases, medical conditions, gastro-intestinal and urinary tract examinations—it is deemed unnecessary to preserve or retain the x-ray films for a longer period than six months after their exposure.

This is, however, not in any way to be construed as discouraging the preservation of films of specially interesting or unusual conditions, as these are to be preserved because of their value for comparative study and for teaching purposes, and it is further

RESOLVED, that referring physicians desiring to preserve the x-ray films of their own patients, be encouraged to do this, and it is hereby declared permissible and proper practice for roentgenologists to deliver the films to the referring physicians in such cases, and it is further

RESOLVED, that a copy of these Resolutions be sent to The Bulletin of The Chicago Medical Society, The Illinois Medical Journal, The Journal of the American Medical Association, Radiology, and the American Journal of Roentgenology, for publication, and to the American College of Radiology, the American College of Surgeons and the American College of Physicians with request that the same be published in their official journals, and to the Sections on Radiology of the American Medical Association and of the Illinois State Medical Society, and to the Chief of the Fire Prevention Bureau of Chicago and the Underwriter's Laboratories, Inc., of Chicago, and to the editors of Hospital Management and Modern Hospital.

#### OBITUARY

Dr James Winfield Cokenower (Associate), Des Moines, Iowa, died April 16, 1929, of pneumonia, aged 75.

Dr Cokenower graduated from the Keokuk (Iowa) Medical College in 187, and later received the medical degree also from the Kentucky School of Medicine (Louisville) in 1882. He later did postgraduate study at the Kentucky University Medical Department.

Hospital. He was an ex-president of his County Medical Society, a member of the Iowa State Medical Association and a member of the American Medical Association. He had been an Associate of the American College of Physicians since 1925.

Dr Cokenower was ex-professor of orthopedics at the Drake University College of Medicine (Des Moines), and formerly on the staffs of the Iowa Methodist Hospital and the Mercy Hospital. He was an ex-president of his County Medical Society and a member of the American Medical Association. He had been an associate of the American College of Physicians since 1925.

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'Charles Stanley McVicar (Fellow), Rochester, Minnesota, died June 29, 1929 of coronary sclerosis, aged 49 years.

Dr McVicar was born in MacGillivray Township, Middlesex County, Ontario, attended the public and high schools in Ailsa Craig and Parkhill. At the age of nineteen, he enlisted with the Canadian forces for service in South Africa. On his return to Canada, he entered the Western Medical College where he studied for two years from 1902 to 1904. The last two years of his medical course were taken at the University of Toronto Faculty of Medicine, where he was graduated as Silver Medalist in 1907. On completion of his hospital training, he engaged in practice in Toronto and was associated with the teaching staff of his Alma Mater.

During the World War, Dr McVicar again served with the Canadian forces this time in Salonika, where he was mentioned in dispatches for

distinguished service by General Milne. He also served as Lieutenant Colonel, and as Chief of Medicine in the Orpington General Hospital, England. From here he was called to Toronto to take charge of the Christie Street Orthopedic Hospital, which was the central orthopedic institution of the Canadian Army.

In January, 1921, Dr McVicar accepted an invitation to join the Staff of the Mayo Clinic. Owing to his outstanding ability, he was soon made head of a section in Gastro-enterology and Associate Professor of Medicine. The Mayo Foundation, Graduate School of the University of Minnesota.

His broad view point in medicine, his firm, sincere and fearless character, likeable personality, his love of home and capacity for friendship marked him for leadership. He was an excellent speaker and was in great demand for medical meetings throughout the United States and Canada. He was a member of the American College of Physicians since 1926.

(Submitted by Dr George E. Brown, Rochester, Minn.)

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Edgar Orrin Crossman (Fellow) Washington, D. C. died June 21, 1929, at his summer home in Bedford, N. H., of pneumonia, aged 62 years.

Dr Crossman was born at Ludlow, Windsor County, Vermont, attended the common schools at Plymouth, Vt., spent two years at the New Hampshire State College and received his medical degree from the University of Vermont in 1887. Early in his practice he began to specialize in internal medicine and neuropsychiatry. He was in charge of the Department of Nervous

Diseases at the Clifton Springs (N Y ) Sanatorium from 1891 to 1894, medical director of the Markleton (Pa ) Sanatorium from 1899 to 1903, medical director of the Lake View Sanatorium (Burlington, Vt ) from 1916 to 1918, and more recently had been appointed medical director of the U S Veterans Bureau

Dr Crossman had always been interested in keeping abreast of all developments in medical science, as evidenced by his pursuit of several postgraduate courses at such institutions as the New York Postgraduate Medical School, Harvard Medical School, Boston Psychopathic Hospital and the University of Michigan. He contributed a number of articles to various medical journals, and served as President of the New Hampshire State Medical Society. He was also a Fellow of the American Medical Association, a member of the Hillsboro County Medical Society, a member of the American Psychiatric Association, and was elected to Fellowship in the American College of Physicians on April 8 1929. He further held the commission of Lieutenant Colonel in the Medical Reserve Corps of the U S Army.

"Caution, courage, acumen, and honesty were the outstanding characteristics of Dr Crossman's character. He was lovingly called "the old fox." Such strength of character was never more needed in any position than when Dr.

Crossman was directed to take charge of the Medical Service of the United States Veterans Bureau in 1924. He brought and gave to the Bureau not only mind and courage, but sound medical training and great technical knowledge. The Medical Bulletin of the Veterans' Bureau was published by his order. Without money, he installed the spirit of research into a half hundred hospitals. He fought for recognition of and proper recompense for the doctors under him. He instituted schools for the better training of his physicians. He constantly strove to have these physicians maintain the high ideals of the medical profession. His conception of the prime function of the Director of the Veterans Bureau was to secure for the doctors in the field both the men and materials required for their work. Thus he raised the Veteran's Bureau's hospitals above mediocrity. He was active in creating and most adroit in using the Director's Medical Council. He was untiring in devising ways to improve the Medical Service, but worked hardest to maintain those improvements which had been inaugurated. He was a great leader. His best thoughts seemed so simple and direct that they were not always recognized as great. Thousands of lives have been saved and other thousands have been improved by his foresight and wise administration."

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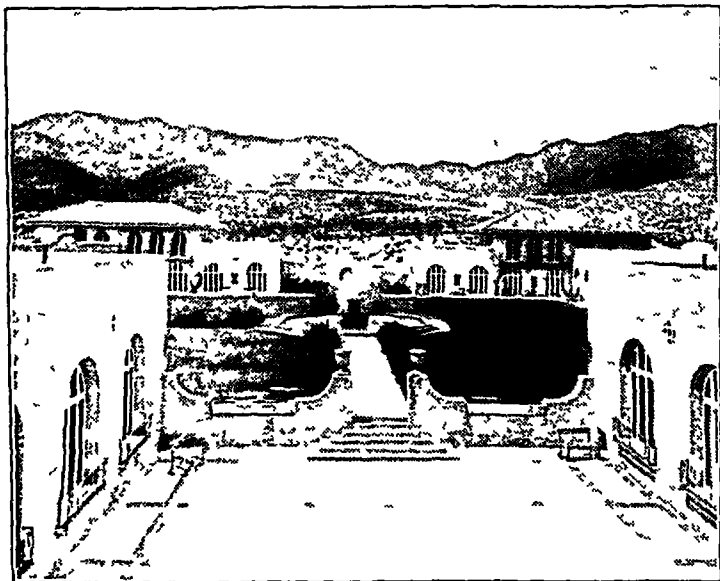
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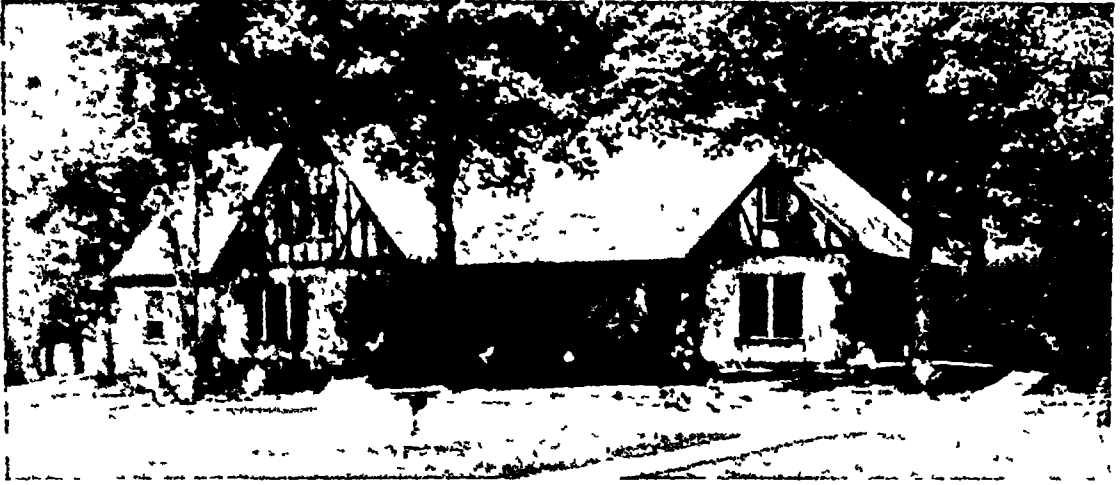
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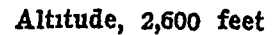
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The Journal will make an especial feature of the reviews of monographs and books bearing upon the field of Internal Medicine. Authors and publishers wishing to subject such material for the purposes of review should send it to the editor. While obviously impossible to make extended reviews of all material, an acknowledgment of all matter sent will be made in the department of reviews.

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ALFRED SCOTT WARTHIN, M D  
Pathological Laboratory, University of Michigan  
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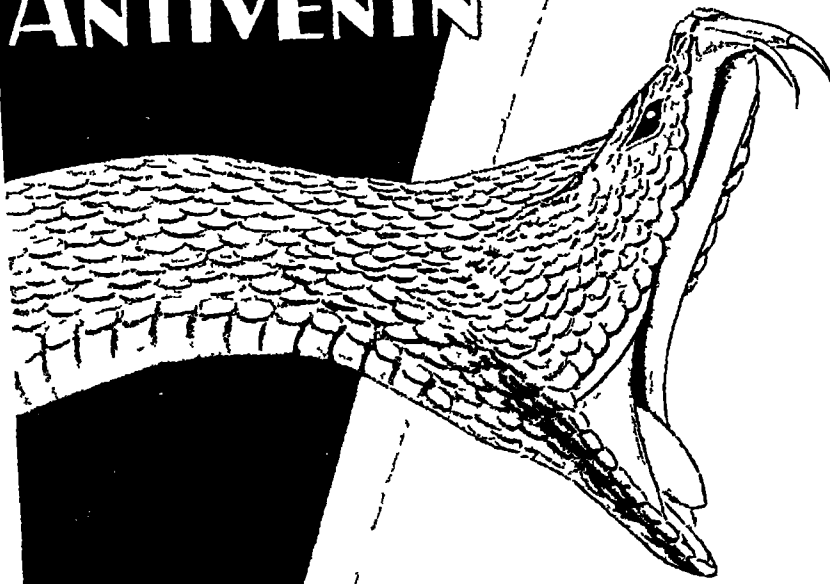
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by the General Practitioner)\*

By LEWIS F. BARKER, M.D., *Baltimore*

**B**Y affective disorders, I mean pathological disturbances of the feeling-tone, the mood, and the emotional life of patients. There are many varieties of these disorders, but I shall limit my discussion at this time to the milder depressions and the milder elations that are often observable in patients of the so-called cyclothymic or elative-depressive constitution. Though such affective disorders are usually easily recognizable by practitioners who have been trained in neuropsychiatry, they are undoubtedly often overlooked or entirely misunderstood by physicians and surgeons who have had but little experience in the study of abnormal mental states. An outspoken depression or melancholy of severe grade, with delusions of poverty, of unworthiness and of sin and with ideas of, or attempts at, suicide, will scarcely escape recognition, even by the tyro, nor will an exaggerated expansive state with great elation, with delusions of grandeur, with extravagant self-appreciation, with marked push of talk and pressure of activity and with aggressive attacks upon the surroundings be likely to go undiagnosed.

It is very common, however, to find that the milder depressive and expansive states, as well as the mixed states in which symptoms of elation and of depression are combined in the same patient, are wrongly diagnosed, very often the symptoms are attributed to accidentally associated somatic disorders, or to mere neurasthenia or hysteria. A few case-histories, briefly epitomized, will illustrate some of the types of disorder I have in mind better perhaps than longer and more detailed descriptions.

## CASE I

### *Second Attack of Depression in Patient Who Attributed Her Symptoms to Somatic Disorder*

Mrs L., act 52. *Complaints* "nervous" for preceding 10 months, inability to make decisions, loss of interests, tendency to worry; tinnitus, insomnia, anorexia, constipation alternating with diarrhoea, burning in rectum.

She received treatment in several hospitals and sanatoria but without relief of symptoms. She consulted a long series of physicians, as well as a Christian Science healer. She was operated upon for hemorrhoids and rectal fissures, she was treated in one hospital for suspected amebic dysentery, in another for spasm of the colon and mucous colitis associated with abdominal pain. Patient attributed her sufferings partly to fright in an

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automobile accident, partly to her rectal operation

One friend tried to cure her by taking her on visits to the slums and showing her the intense poverty of people who were even worse off than she thought herself to be. Bromides and luminal have been taken in large quantities for the nervousness and insomnia. Patient has grown greatly discouraged, wishes she could die.

Diagnostic survey revealed, in addition to the affective disorder, some oral sepsis, a mild secondary anemia, a spastic colon, and moderate obesity (20 pounds over ideal weight).

On inquiry it was found that 23 years earlier (at the age of 29) she had passed through an attack of depression accompanied by long periods of weeping from which she gradually recovered without hospitalization.

## CASE II

### *Fourth Recurrent Depressive State in Patient of Cyclothymic Constitution*

Mrs. H., aet. 40. *Complaints* "nervous breakdown, tenseness without power to relax, sensation of drawing in and about eye balls, inability to eat and loss of 50 pounds in weight; insomnia, headaches, weakness, weeping spells, irritation because impossible to rise above her symptoms, difficulty in making decisions, several abdominal operations without relief of symptoms, greatly discouraged."

Diagnostic survey revealed, in addition to the affective disorder, chronic tonsillitis, intestinal stasis, a mild cystitis, slight hyperthyroidism and profound undernutrition (46 pounds below calculated ideal weight).

A study of the earlier history showed that the patient had suffered from three attacks of depression in the preceding sixteen years and that her mother had also been the victim of recurrent depression.

nature. She cannot understand her present sadness, fatigability, loss of interests, and feelings of insufficiency.

## CASE III

### *Sixth Recurrent Depressive State with Familial History of Depression*

Mrs. T., aet. 46. *Complaints* "Bad teeth and tonsils; great nervousness, insomnia, weeping spells, constant feelings of physical fatigue and exhaustion, panicky feelings, tenseness, always anxious."

Diagnostic survey revealed, in addition to her affective disorder, severe oral sepsis (eleven infected teeth), chronic constipation and hemorrhoids, uterine myoma, low blood pressure and slight hypothyroidism.

A close analysis of the patient's previous history showed that she had passed through no less than five periods of depression. Each attack had lasted many months. In some of her depressions she harboured definitely suicidal ideas and required sanitarium treatment. In one attack, while under treatment in a hospital for nervous diseases she ran away, returning to her own home "to fight it out by herself." One of her uncles committed suicide while in a period of depression.

## CASE IV

### *Expansive Dynamic Personality with Recurrent Depressive "Slumps."*

Mr. G., aet. 68, a prominent financier of prodigious energy and activity, returns to the hospital at intervals of a year or two, usually with some somatic complaint (joint pains, sinus troubles, digestive disturbances), but really because of recurrent periods of exhaustion, loss of usual feeling of vigor, let down of interests and mild depression.

Diagnostic surveys, at one or another visit, have revealed, in addition to the affective disorder, oral sepsis, slight paranasal sinusitis, hemorrhoids, moderate obesity, anginal pains, slight anemia, low blood pressure, benign prostatic hypertrophy, and slight hypertrophic osteoarthritis.

Studies of the life-history of the patient show that he has achieved noteworthy success in the business world, is much beloved

and admired, and his hosts of friends to whom he writes long, jolly letters in a large, bold hand. Except in what he calls his "slumps," he is exceedingly optimistic and happy shows great pressure of activity, travels much (sometimes 35,000 miles in one year), exhibits "push of talk," writes jingles and wishes to "stick around the good old world for years to come enjoying good health and never to become an extinct volcano." In other words, when he is what he calls "well," he has a very dynamic expansive personality pushes himself far beyond his strength, but gets great satisfaction out of accomplishment. He admits that nobody in the world can control him unless he controls himself. His wife and friends are powerless to stop him in his tremendous physical and mental activity which amounts to a veritable "drive."

His brother once spent several months under my care in a hospital because of an affective disorder in which there was marked loss of interest, fatiguability and depression.

#### CASE V

##### *Mixed State. Predominantly Expansive Psychosis with Depressive Components*

Mrs O, aet 56 *Chief Complaints* "fear of cancer, insomnia, red and watery eyes, sinking spells." She has attacks called "vasomotor crises" in which there is tingling of the fingers, cold extremities, flushing of the face, palpitation of the heart and tachycardia with some rise in blood pressure.

A diagnostic survey revealed, in addition to the neuropsychiatric malady, a slight chronic arthritis, obesity, and a refraction error in the eyes.

The patient maintains that she must rest quietly in bed for fear of precipitating a "vasomotor crisis." Except that she is obese she looks as though she were in blooming health, her eyes are very bright and somewhat watery and she has a high color. She talks volubly of her symptoms, is obviously egocentric, and laughs and jokes much. She writes many rhymes and jingles, which she dedicates to her physicians. The nursing problem has been very difficult, she has had

some seven changes of special nurse, in as many weeks of observation. In several instances she has, herself, demanded change of nurse because of "inattention," "failure to carry out orders," or "unfriendliness", on the other hand, three of the nurses begged to be relieved of the care of the patient because of excessive and sometimes unnecessary demands, her sarcastic remarks and her general attitude that became to them unbearable. All seven of these nurses were regarded as well-trained and had not experienced any difficulty in the nursing of other patients. The nursing problem became so acute that transfer of the patient to a closed institution is contemplated. The patient's son has several times been under treatment in asylums because of maniacal outbreaks.

#### RECOGNITION OF THE DEPRESSIVE STATES

*Negative Feeling Tone*—The affective life in depressed patients is dominated to a greater or less degree by negative feeling tone. The patients complain of discomfort and torture (worse they say than physical pain) and of loss of capacity for pleasure. They are sad, blue, and gloomy. They are pessimistic and see everything through dark coloured spectacles—not only their own lives but also their surroundings. They become greatly discouraged, and complain bitterly of loss of vigor and of normal interests. They feel insufficient for their everyday duties, find it difficult to make decisions, and tend to blame themselves for failure to surmount their difficulties. There is usually a diurnal variation in the symptoms, the patients being more depressed in the earlier parts of the day.

*Anxiety*—Many of the patients complain of a vague general anxiety, others localize feelings of anxiety or



oppression in the precordial region, in the head, in the epigastrium or elsewhere. They interpret these anxious feelings as symptoms of some serious or incurable disease or, perhaps, as evidence that they will lose their minds.

*Slowing of Thought and Speech and Emergence of Pathological Micromanic Ideas*—In the milder affective disorders there is no clouding of consciousness, no disorientation, and no failure of comprehension. The patients may complain, however, that their thinking is slowed, and they may talk less and more slowly than when they are well. These symptoms help to fix the ideas of inadequacy and of baseness in their minds and to increase the tendencies to self-depreciation and self-blame. Trivial errors or excesses are raked up out of the past and given undue importance as causes of personal or of familial unhappiness. Pathological ideas of unworthiness, of poverty, and of sin may emerge in consciousness and exaggerate the mental torture. The patients assert that they are good for nothing and feel that the condition is humiliating. They say that everything is a burden to them and that they are a burden to others. Often they may become more and more inert and tend to avoid contacts with family, friends, or business associates. In the severer depressions, suicide is always a great danger; even in the milder depressions, the family and the attending physician should always be on the watch both for suicidal ideas and for suicidal impulses.

*Deceptive Bodily Symptomatology.*—Area of pain or of paraesthesia may frequently be complained of and may

mislead the attending physician. These symptoms may excite the suspicion of angina pectoris, of multiple neuritis, of tabes, of brain tumor, or of serious disorder of the digestive, the circulatory, or the urogenital system.

#### RECOGNITION OF PATHOLOGICAL EXPANSIVE STATES

*Domination by Expansive Moods and Emotions*—The affective life in exalted patients is the counterpart of that observable in depressed patients. The feeling-tone is positive rather than negative. The patients appear overhappy and overjoyful, rather than sad. They exhibit "push of talk," laugh and joke on the slightest provocation and often tend to be over-friendly and overactive. They are, however, subject to sudden and often inexplicable changes of mood and not infrequently they show insufficiently motivated irritability, anger, and overaggressiveness toward those about them. Emotional instability is characteristic of them and their euphoric states may suddenly, and without rhyme or reason, give place to episodal states of depression. The expansive patient, as a rule, gives the impression of a preternatural freedom and feeling of well-being; he sees everything through rose-coloured spectacles, is over-optimistic and outspokenly egocentric. He is likely to dress extravagantly and often fantastically. Even in the presence of difficulty and sorrow, he may maintain a holiday mood and so appear unsympathetic and perhaps heartless through failure to manifest, even briefly, consideration for the misfortunes of others.

These patients often exhibit a loss of sense of the value of money and spend it foolishly

*Acceleration of Movement, Thought and Speech, Distractibility, and Emergence of Pathological Grandiose Ideas*—Expansive states are characterized further by pressure of activity, increased ease and rapidity of associations, unusual distractibility, and often by the manifestation of exaggerated ideas of self-importance and power. The patients are often harder to live with than the mildly depressed, for they wear out their families and sometimes also exhaust their few friends

These patients are prone to be exceedingly alert and over-active, they are over-talkative, restless and must be doing something all the time, everything seems easy for them, and they behave as though they were immune from feelings of fatigue, surprising their companions by their unremittent energy and by their endurance. They often seem vain, are rather over-sure of themselves, and frequently exhibit erotic symptoms. The attention is likely to be superficial and to be easily shifted from one object or idea to another. Their trains of thought suggest the absence of normal inhibitions, they are often incapable of prolonged concentration upon a goal, they tend to be easily distracted, turning their attention very easily from one topic to another; they may thus exhibit a true "flight of ideas." Moreover, they are prone to make puns, to rhyme, to be subject to associations by sound, and to use in close juxtaposition words that begin with the same letter (alliteration)

The elated patient may write a

great many letters to friends and acquaintances, often in a very large hand, with excessive spacing of the single enlarged letters, many underlinings, and frequent exclamation points. Indeed, in some patients, the predilection for excessive letter-writing may be more striking than the push of talk. Sometimes, there is marked literary productivity, only recently I have read a novel that made me feel sure that its author must have written it during a period of pathological expansiveness because of the superficiality of the associations, the frequency of alliterative phrases, the abundance of sound associations, and the excess of words and phrases printed in italics

*Bodily Symptoms of Exalted Patients*—Patients who are over-expansive often look as though they were enjoying unusually good health, they appear full-blooded and happy, their eyes are very bright and sometimes watery, they may eat ravenously, and they often give the impression of living much more fully than their fellows. Some of them, however, complain of headaches and of insomnia, moreover, on closer examination, the futility of their performances despite their excessive activity is sometimes easily demonstrable

#### RECOGNITION OF MIXED DEPRESSIVE AND EXPANSIVE STATES

Aside from the fact that depressive states and expansive states may be met with in the same patients at different times in their lives, sometimes indeed alternating with considerable regularity (hence the term "cyclothymia"),

it should be borne in mind that many persons exhibit certain depressive symptoms and certain expansive symptoms simultaneously. These mixed states may be particularly puzzling to the physician who has had but little psychiatric training, and among professional psychiatrists there is much difference of opinion as to their proper classification.

Some patients while predominantly depressive also exhibit irritability, querulousness and aggressiveness suggestive of expansive states. Another group with markedly negative feeling-tone may exhibit motor agitation, egocentricity and hypochondriacal traits and because of the latter make insistent claims upon those about them. And a third group of patients obviously depressed may also manifest distractibility and flight of ideas.

On the other hand, one may see a predominantly expansive patient of euphoric mood, who exhibits, associated with this, a certain psychomotor retardation. In a second expansive patient there may be exaggerated self-appreciation and flight of ideas, but along with these symptoms a certain shyness and bashfulness. In still another expansive patient, though the mood may be exalted, there may be no flight of ideas but rather lessened associative activity—the so-called “unproductive elation”.

Still other varieties of “mixed states” have been described. The whole matter is still obscure, defying satisfactory attempts at nosological classification. In some of these states we probably have to deal with constitutional illness of the syntone with the

schizoid temperament and of the pyknic with the asthenic habitus.

### CONCLUSIONS

Among the patients that apply to general practitioners for diagnosis and treatment, many present, in addition to their somatic abnormalities, the problems of affective disorders of lower or higher grade, often overlooked or entirely misunderstood by physicians or surgeons without neuropsychiatric experience. The recognition of such affective disorders and their assignment to their proper nosological positions are of importance for prognosis and for adequate care and treatment. The thorough schooling of medical students in the main facts and principles of modern psychiatry and the more extensive utilization of neuropsychiatric consultants by physicians and surgeons who do general work would seem to be desirable.

In the treatment of the affective disorders, it should be made plain that the depressive phases are circumscribed in time and that they have to “run their course.” I like to think, though, that by general hygienic measures we may do something toward shortening the duration of a depression. The patients, except when their disorders are very mild, are best treated away from home, without visits or letters from family or friends, under good nursing care, with close supervision by physicians who understand these disorders, who build up the general health, who protect from forms of therapy that are harmful rather than helpful, and who give all justifiable symptomatic relief until the depression disappears.

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# Tuberculosis Theses; Diagnostic, Prognostic, Therapeutic\*

By LAWRASON BROWN, *Saranac Lake, N Y*

**A**RTICLES of faith to which one may subscribe or from which one may dissent are of value in many activities of life. To the beginner in an art they point out a ford across troublous and swift waters. That other easier and safer fords are not to be found or, indeed, do not already exist is not denied but here at least is one. To him who has long practised the art they seem, in part at least, axiomatic and tiresome, or else not to be accepted. Their power to arouse discussion, to lead to thought, to foster healthy disagreement, is all that their author desires. That he will be able to subscribe to them all in some months he doubts, but today they represent what he finds from his experience, colored, no doubt, by that of many others, to serve him as a guide for action.

These theses were published in part some ten or twelve years ago and the author has been surprised to see how extensively he has had to revise and to add to them.

## I DIAGNOSTIC THESIS.

1 An appearance of ruddy health does not exclude tuberculosis

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2 In any patient with constitutional symptoms, no matter of what he complains, the possibility of tuberculosis must be kept constantly in mind.

3 Prolonged and intimate exposure at any time of life, but especially in childhood, either in home, workshop, or office, is vastly more important in diagnosis than "unassociated" or "non-contact" heredity.

4 When demonstrable pulmonary tuberculosis first develops has never been determined but probably it is nearly always discoverable before the twentieth year.

5 Prolonged contact with tuberculosis may and often does lead to infection, but debilitating conditions are usually necessary to cause this to develop into clinical tuberculosis.

6 Among the debilitating conditions the hyperenthusiastic mode of life, formerly confined to college, now prevalent in high schools, the exposure to cold due to insufficient modern dress and the limitation of the diet during the period of growth, particularly in young girls, play an important part in the development of disease.

7 Constitutional or general symptoms suggest the diagnosis of tuberculosis, while the localizing symptoms point out the organ involved.

8 The history or presence of certain complications, such as fistula-in-

ano, pleurisy, adenitis, a discharging ear coming on painlessly, are all strongly suggestive of tuberculosis

9. Pleurisy with effusion, not attributable to other causes, demands a diagnosis of suspected pulmonary tuberculosis and treatment for a time at least

10. A diagnosis, tentative at least, of pulmonary tuberculosis must be made whenever an individual coughs up a drachm or more of blood that cannot be proved to be due to other causes (e.g., mitral stenosis, etc.)

11. A positive diagnosis of pulmonary must be made whenever hemoptysis of a drachm or more and pleurisy with effusion both occur

12. Familiarity with a patient lends him no immunity to tuberculosis. Your patients, your friends, your family are as prone to contract and to develop pulmonary tuberculosis as hundreds of others

13. Symptoms indicate that a patient is sick, while physical signs\* point out only the mischief that has been done

14. Symptoms are a better and more accurate guide to activity than are physical signs

15. Symptoms without abnormal physical signs demand treatment, while abnormal physical signs without symptoms require often only careful watching

16. While the temperature and pulse may be normal, slight but persistent rise in temperature and slight increase in rapidity of pulse are often present early in the disease

17. The "usual" weight of a patient who develops pulmonary tuberculosis is frequently ten pounds below the standard weight for his height and age.

18. Failure to interpret rightly the significance of symptoms, or to detect the presence of abnormal physical signs, can be condoned, but failure to ask for and to examine the sputum repeatedly in any patient with chronic cough is inexcusable

19. Absence of tubercle bacilli in the sputum suggests only that bronchial ulceration is not present.

20. When diagnosis leans heavily upon the sputum examination at least 3 or 4 typical tubercle bacilli must be found

21. The importance of the usual negative physical examination in the exclusion of pulmonary tuberculosis has been over emphasized

22. No single physical sign is pathognomonic of pulmonary tuberculosis

23. Auscultation and roentgenography are the most important procedures in the detection of abnormal physical findings

24. Inspection may reveal localized retraction of the chest wall and limitations of the chest movement.

25. The detection of râles by auscultation of the inspiration following cough is the most important stethoscopic procedure in the detection of physical signs of early pulmonary tuberculosis

26. Localized râles, usually moderately coarse, in the upper third of the chest are exceeded in importance only by tubercle bacilli in the sputum and

\*These Include X-ray Findings

by changes upon the roentgenographic film

27 Such râles may be due also to a rare type of pneumonia, to a clearing acute bronchitis, or to localized pulmonary edema

28 Changes in percussion and in the relative length, quality, and intensity of the inspiration and expiration are less helpful and less easy to detect

29 Krong's tone planes, Rivière's bands of impairment and Pottenger's muscle spasm, while helpful to some, have not proved of great value to many investigators

30 Measurements of the vital capacity of the lungs are often, probably usually, of little help though possibly of no harm in patients with early tuberculosis

31 The importance of any physical sign is greatly increased by its persistence in one definite area

32 The extent of disease as determined by physical signs is usually less than that revealed by the x-ray film (roentgenogram)

33 Abnormal physical signs in the upper third of one lung should be considered as due to pulmonary tuberculosis until proved not to be, while those at the base should be looked upon as non-tuberculous until definitely proved so

34 Tubercle bacilli alone determine that a basal lesion is tuberculous

35 Abnormal physical signs should not be stated to be absent until after a second examination several days later

36 No pulmonary examination is complete without a study of the x-ray film (roentgenogram)

37 The slighter the lesion the better must be the roentgenograms

38 Abnormalities on a single film often fade into a normal picture when viewed stereoscopically Hence in early diagnosis place your dependence upon good stereoscopic films

39 When diagnosis rests upon the interpretation of the roentgenogram, the mottling, a sine-qua-non, must be irregularly distributed ("parenchymatous" lesion), as the linear arrangement ("peritruncal" lesion) while occurring in pulmonary tuberculosis is insufficient evidence

40 The fluoroscope, valuable for the study of movement, both normal and pathologic, and for its aid in the treatment by artificial pneumothorax, fails often to reveal slight lesions plainly evident upon the roentgenogram

41 The extent of disease as revealed by the film exceeds in the majority of cases the extent inferred from the usual abnormal physical signs

42 Extensive (moderately or even far advanced) pulmonary tuberculosis may be diagnosed from the roentgenogram while the usual physical signs remain slight or inconclusive

43 A parenchymatous x-ray lesion is present in 96 to 98% of all cases in which tubercle bacilli occur in the sputum

44 Tubercle bacilli may occur in the sputum when a parenchymatous lesion cannot be found

45 In the diagnosis of pulmonary tuberculosis the evidence offered by the film usually greatly outweighs that presented by the usual physical examination but the opposite holds true for

many non-tuberculous pulmonary diseases

46 The roentgenogram is even more important in the diagnosis of pulmonary tuberculosis in early (infancy, childhood) than in adult life

47 The presence or absence of a complicating intestinal tuberculosis can be determined with accuracy only by roentgenologic study

48 In every patient with extensive physical signs and no tubercle bacilli in the sputum, the evidence in favor of the diagnosis of pulmonary tuberculosis should be considered and reconsidered

49 Laryngeal infiltration or ulceration, limited to one side in any patient with doubtful pulmonary findings, is suggestive evidence of the presence of pulmonary tuberculosis

50 When sputum is lacking or when tubercle bacilli are absent on repeated examinations, the possibility of the presence of bronchiectasis, sinusitis, chronic pulmonary infection, hyperthyroidism, syphilis, endocarditis and influenza, and more rarely pulmonary tumor and Hodgkin's disease, should be borne in mind

51 Sero-diagnosis has afforded little help in diagnosis

52 No modification of the tuberculin tests as yet devised differentiates clearly clinical tuberculosis that demands vigorous treatment from non-clinical tuberculosis that requires only a God-fearing life

53 *Apart from tubercle bacilli*, two or more of the following five data are necessary for a positive diagnosis while the absence of all five is necessary for a negative diagnosis of pulmonary tuberculosis

1 Tubercle bacilli in the sputum

2 Hemoptysis of a drachm or more due to no other cause

3 Pleurisy with effusion due to no other cause

4 Moderately coarse râles above the third rib and third vertebral spine, and

5 Mottling, irregularly distributed (a parenchymatous lesion) in the same area on a well-taken film

53 It may be impossible to determine definitely the presence or absence of clinical tuberculosis, even after a study of two to three weeks

## II PROGNOSTIC THESES

1 The uncertainties of prognosis decrease rapidly after the first year of disease but are ever present

2 He who promises a patient what is unattainable injures himself more than the patient

3 He is most dogmatic who verifies least often his prognosis. Dogmatism and brief observation are boon companions

4 Recovery in pulmonary tuberculosis like recovery in carcinoma, can occur in the apparently hopeless, but does occur very rarely

5 Whether physician or patient, he who is deceived by the "false convalescence" of Laennec, justifies the use of the term

6 Whoever suffers relapse from unavoidable adverse conditions does better than he who relapses without discoverable cause

7 The prognostic significance of race depends more upon the habits of



the individuals than upon other racial characteristics

8 Resistance to clinical disease, largely lacking up to the fourth month of life, increases from the first year onward, and from about the sixth to the fourteenth year is stronger than in adult life. It may persist into old age, when, however, the recuperative powers are at a low ebb

9 Lack of self-restraint often spells death

10 Puberty and the menopause have less bearing upon the disease than pregnancy, especially repeated, frequent pregnancies, and hence marriage for women increases the uncertainties

11 Tuberculous parents (when the child is under 3 or 4 years of age) increase incalculably the chance of infection. Hence the exposure to family infection has often been transferred to inheritance, which beyond this exerts no definitely proved influence

12 The mentality and characteristics of the patient's family, their ability and willingness to help in his recovery by self-sacrifice over long periods of time, are most important. Therefore, recovery in the midst of the family is the most favorable recovery

13 Poverty snatches recovery from the grasp of many a patient but money is only an adjuvant, not a means to cure

14 He, who has worked indoors, does better under treatment ceteris paribus, than he who has always seen the light of the sun in God's fresh air

15 He works longest who works easiest, that is he who returns to his former occupation when congenial and not unduly taxed by sudden great effort and who faces his living with least ex-

ertion and worry, avoids relapse most often

16 Recovery in a climate in which a patient is to live, especially if accomplished at home, bespeaks greater longevity than immediate change of climate on arrest of disease. Climate may be only a minor factor in this effect

17 He who is methodical and not lethargic, cheerful and not over sanguine, firm and not stubborn, educated about relapse and not ignorant of nor indifferent to the mistakes and failures of others, self-reliant and not selfish, possessed of imagination and of self-control in the worship of Bacchus, Venus and Mercury, grasps easily and surely his problem and solves it more successfully

18 A sudden onset with acute symptoms bespeaks an earlier diagnosis than an insidious or catarrhal onset and hence treatment is begun earlier and life is more often prolonged

19 An acute onset with extensive signs of disease or with severe and protracted symptoms points to a prolonged illness or to an early fatal termination

20 The consumption of the body, with or without fever, indicates that assimilation is failing, and when steady and continuous is a priori evidence of poisoning of the body cells, betokening a serious outcome

21 The continuous gain of weight on an ordinary diet is an indication of favorable progress but can occur with advancing disease

22 Assimilation depends primarily upon ingestion, and "poor eaters" with

strong antipathies to milk, eggs, and meat, do badly.

23 Digestion is the keystone of the prognostic arch

24 Fever is the most certain symptomatic sign of progressive disease and its chances of disappearance are inversely proportional to the length of time it has persisted

25 Persistent high temperature under appropriate treatment is grave

26 Frequently recurring febrile attacks, even of short duration, indicate advancing disease

27 A subnormal temperature when other things are favorable is of little moment especially in cold climates

28 The pulse rate, together with the temperature and weight, form the prognostic triad

29 A pulse rate constantly over 100 when the patient is at rest in bed is of bad omen when not due to digestive disturbances

30 Hemoptysis as an accident in the course of the disease is of little moment but when accompanied with fever, cyanosis, dyspnea, or tachycardia, is most grave. It is a favorable sign only when at the onset it fills the patient with the fear of God and a determination to obey orders

31 The outcome depends as much upon what the patient has above his collar as upon what he has below it

32 Nervousness that leads to marked dyspepsia or to excessive fear leads also toward the grave

33 Dyspnea may be the only pronounced symptom of acute miliary tuberculosis of the lungs

34 Uncontrollable excessive cough is the worst form of over exercise

and favors a quick deterioration of the bodily resistance

35 Cessation of menses indicates a weakening of the vital forces, a return of them an increase

36 No urine or serum test is of prognostic value in early tuberculosis, but at times the urochromogen or diazo reaction may afford some aid in far advanced stages

37 Arneith's polymorphonuclear picture, Medlar's leucocytic count, Westengren's sedimentation test have helped some workers

38 A positive skin tuberculin test under the age of two indicates often an active tuberculosis. In youth, adult life and old age no tuberculin test differentiates clearly and surely active from arrested disease

39 Physical signs tell by inference what has happened in the lungs, symptoms what is happening. The general condition is more important in prognosis than the physical signs or the history

40 The most certain thing about the physical signs of "activity" or "softening" is their uncertainty

41 Disease at an apex usually heals more readily than disease located elsewhere, but it must be in the real anatomical apex

42 Extent of disease usually registers the time element, intensity the acuteness

43 Extent of disease postpones arrest longer than localized intensity

44 Extensive disease with short duration of symptoms suggests prolonged presence of the disease and possibly weakening of the resistance

45 Scattered foci, discovered soon

after the onset of symptoms, betoken lack of resistance

46 Granting the diagnosis, slight deviations in breathing or percussion are the most favorable physical signs

47 The condition of the opposite side in advanced disease affects seriously the prognosis

48 Increase of physical signs, with lessening of localizing and general symptoms and gain in weight, does not necessarily indicate an advance of disease

49 Improvement and even arrest can occur without change in the physical signs

50 Serial roentgenograms reveal best the progress of the disease

51 He usually does best whose serial roentgenograms,—other things being equal,—show no further change

52 Prognosis is more uncertain as long as the roentgenogram indicates change in the process for worse or even for better

53 Mottling with soft cottony edges on a well-taken roentgenogram is very often associated with a recently active process and hence demands a more guarded prognosis

54 As soon as the disease-process extends from the apex below the third rib, the seriousness of the case greatly increases

55 A cavity detected only by roentgenologic study is less serious than one discovered by percussion and auscultation but both are serious

56 The greater the quantity and probably the greater the fluidity of the process when persistent, the less favorable the prognosis

57 Tubercle bacilli in the sputum indicate bronchial ulceration and the

larger the number possibly the greater or more acute the ulceration, but enormous masses may occur in favorable cases

58 The arrangement of the tubercle bacilli in clumps, chains, parallel pairs, or their occurrence in phagocytes is of uncertain prognostic moment

59 Pneumothorax is always serious and often ushers in a fatal stage of the disease

60 Secondary tuberculous enterocolitis, detected early, and treated appropriately, often retards but slightly the recovery

61 Duration of treatment of less than three months is of little permanent help, while three or four years of treatment may assure an arrest

### III THERAPEUTIC THESES

1. The tendency to recovery in some patients is so marked that it ensues in spite of the most injurious treatment

2 That disease is rare for which the medical profession can do as little as for steadily advancing acute pulmonary tuberculosis

3 The treatment of pulmonary tuberculosis demands little knowledge of drugs but much about the immediate and prolonged education of the patient

4 Whatever advantages the sanatorium, and the class system and certain physicians possess, and they are many, lie in the fact that these institutions are really teaching institutions and the physicians are educators

5 The marked tendency to temporary arrest or quiescence even in advanced stages rests upon the brow of

the tuberculous evil doer like the curse of Cain

6 The danger time in tuberculosis, the perils of the "false convalescence" of Laennec, can not be over emphasized

7 The idea that pulmonary tuberculosis, though often easily arrested, is a most curable disease, is a fallacy

8 The time allotted to treatment is usually too short, for recovery is ever longer than onset. The value (possibly the results) of treatment increases as the square of the time, that is, two years are four times as valuable as one, but the struggle lasts often from diagnosis till death

9 The physician must always bear in mind that he can influence the lungs only through the intermediary of the body. Hence besides being an educator he must become an expert in physical training

10 The physician must have imagination, sympathy, firmness, approachableness, as well as knowledge of the disease of the individual patient, his psychological and his sociological condition, and last but not least, of the limitations of his own knowledge

11 Few physicians are temperamentally suited to successfully care for chronic disease, while many can treat successfully acute disease. Pulmonary tuberculosis is a chronic disease

12 The patient is worried, confused, twists what is told him and can master the thousand and one details only by repeated perusals of directions carefully written down. He should not be blamed for the physician's mistakes of omission. Word of mouth, however, conveys to the patient

emphasis and force and directness that tons of tomes cannot

13. At home and abroad, in the desert or on the ocean, in the lowlands or upon the mountains, patients may do well, as they recover anywhere and everywhere, for it matters less where than how they live

14 Fresh air, one hundred times more frequent outside than in the house, depends for its value far more upon the temperature, moisture and movement of the air than upon the presence of any organic or inorganic constituents

15 The skin demands better air than the lungs, for we can breathe with impunity far worse air than we can live in. Hence the lungs are benefited by fresh air no more, no less, than any other organ.

16 The dose of fresh air, an important component of the *vis medicatrix naturae*, must be carefully regulated for the weak and aged, as stimulation, not fatigue, is the goal

17 The development of a fresh air conscience which suffers, when its owner crosses too soon the threshold into the house, aids greatly in recovery

18 For those who spend eight hours out of doors, sleeping out does not hasten recovery, providing they sleep in well ventilated rooms, but for those forced to be indoors during the day it may be a *sine qua non* of continued arrest

19 The sanatorium, the best place in which to treat patients in large numbers, has shown that permanent arrest may follow effectual treatment, the hospital has afforded evidence that direct contagion may in part be con-

trolled, while the dispensary has become the advanced attacking line, so to speak, that carries the warfare into the enemies' camp, that is, into the homes of the tuberculous, and disposes of the wounded in a proper manner

20 The length of stay in these institutions depends upon the object to be attained, for permanent recovery two or three years, for quiescence at least three months, for prevention of infection by far advanced cases, as much as possible of the time between admission and death

21 Give your patient as little food as will serve his purpose and have clearly in mind what this purpose should be—to gain up to, and ten to twenty pounds beyond his usual weight, which is generally ten pounds under what he should weigh for his height and age

22 Remember that too much food may in the end prove as disastrous as too little food, and furthermore that it is a great pity to waste good food

23 See that your patient has a well balanced ration and if you wish him to gain weight, increase his carbohydrates

24 When anorexia appears upon the horizon, and simple tonics cannot dispell the bugaboo, do not fail to resort to fluids and fluids only without a bite to chew.

25 Injury demands rest for repair. Scar tissue forms but slowly

26 Insistence upon absolute quiet and its observance for six weeks affords rest for repair, time for growth of scar tissue and opportunity for the clearing off of areas of disease in the restorable zones. Such short pe-

riods of rest in later stages accomplish no comparable results

27 When such a period of rest has been enforced, exercise can be more quickly increased with less danger of relapse

28 While differences of opinion may exist in regard to the explanation of how rest brings about recovery, none questions its efficacy

29 The period of preliminary rest affords the physician opportunity to assist the patient to think out his problem, which means, when it has been successfully done, that half the battle has been won

30 When general bodily rest fails to aid in arresting the disease, many methods to bring about increased local pulmonary rest have been devised and in many instances have accomplished an arrest of the disease (e g, posture, weights on the chest, various harnesses, phrenicotomy, artificial pneumothorax (including pneumolysis) and thoracoplasty)

31 Exercise should be regarded as a powerful and a dangerous medicine, to be used carelessly never, with impunity by none, and as a deadly drug by all

32. Work for therapeutic purposes is fraught with much danger and is more safely replaced by work which fits the patient for his future (often his former) occupation

33 Since the vast majority of patients must or do seek treatment only in the climate in which they contract the disease, the so-called climatic treatment is of importance to hardly more than five per cent of all patients

34. Change, change of food, change of work, change from work to rest,

change of environment, change of climate, in fact any change that stimulates nutrition sufficiently, helps toward recovery.

35 Those with acute tuberculosis, cachexia, marked dyspnea with cyanosis, advanced nephritis, diabetes with carbohydrate intolerance, intractable diarrhea, extensive laryngeal tuberculosis with dysphagia, or tuberculous pneumothorax are best treated for a time at least in a hospital near their homes

36 It is criminal to advise an untrained patient to seek benefit from climatic change without constant medical supervision

37 Resilient youth responds to strong stimulation while more rigid age requires protection

38 As a rule a patient should be sent to as cold a climate as he can react to and enjoy

39 Beyond the empirical fact that many patients do better for some change, much has been written but little proved about climatic treatment

40 Climates of high altitudes unquestionably exert the greatest physiologic effect upon the human economy

41 There is as yet no accredited specific (like arsphenamine in syphilis) for tuberculosis

42 Drugs may alleviate or even remove for the time being certain localizing and constitutional symptoms but affect in no direct way the disease that produces them

43 Hemotherapy and organotherapy have only historic interest, while serotherapy has greatly disappointed many of its most ardent followers Zomotherapy may be an exception but it is to be used rather as a food

44 Bacteriotherapy, that is, the injection of attenuated (for the species), living tubercle bacilli has given the most promising results so far but immunity so produced is not lasting and not yet safely applicable to man The use of antagonistic bacteria (like the seton of old) is chiefly of historic moment though the activation of one tuberculous focus may bring about quiescence in another.

45 The tubercle bacilli or their products, otherwise known as tuberculin, the most widely used of all so-called specific agents, have not given, when subjected to cold impartial statistical study, the results claimed by the enthusiasts

46 In a few cases remarkable recoveries occur in patients taking tuberculin, which are apparently more than coincidences and tend to keep alive the treatment

47 The time may yet come when by the study of the sera or other means we may be able to select the proper antigen and so to space and to grade the dose, that, having removed tuberculin from the field of empiricism, we can use it more successfully in the treatment of certain cases of tuberculosis.

48 The use of the heavy metals and rare earths in treatment is associated with risk and the results, while striking at times, are uncertain

49 He who deals with statistics upon which the lives of others may depend should have more knowledge of statistical work than will suffice only to compute averages and often erroneously to compare them

# Some Fundamental Clinical Aspects of Deficiencies\*

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## INTRODUCTION

TOWARD the close of the nineteenth century, as the sciences of bacteriology and immunology were becoming well established the dawn of knowledge arose concerning the enormous importance of small amounts of chemical substances for the maintenance of health. It is known today that abnormal amounts, or an improper balance, of highly potent active principles derived from glands of internal secretion, and of vitamins, of inorganic and other substances contained in food, can lead to many sorts of disorders. The secretions of the ductless glands together with materials derived from food must form with blood a suitable environment to bathe the cells of the tissues. This nicely balanced mixture may be altered in myriad ways and if too unsuitable the cells suffer and disease ensues.

Ill health or disease arises either because the organism is affected by the presence of something harmful or by the absence of something beneficial. Infections, intoxications and excess of substances

are examples of the reasons for the former sort of condition. The term "deficiency disease" has been applied by custom to conditions where the essential cause is an inadequate supply of accessory food factors known as vitamins. Deficiencies, however, may be due to a variety of causes acting individually or combined. They may develop among other ways from the lack of an ingredient necessary for the manufacture of a specific molecule (hormones), from disease of organs leading for example to anoxemia and to failure of supply or manufacture of such substances as enzymes or bile. The lack of an element as iron, calcium and iodine, insufficient food or water, or the inadequate supply of protein, certain amino acids and other food components also can lead to a deficiency disease just as much as the lack of vitamins.

Injurious effects also can be dependent upon excesses of some factors that in sparse amounts lead to a deficiency disorder, for example excess of protein, hormone secretions and the ingestion of too much irradiated ergosterol (vitamin D<sup>2</sup>). Thus, for health, the body always requires *optimal amounts* of materials and the absence of harmful factors.

Disorders due to excesses of food, to intoxications and infections, have

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received more attention and are better recognized than many deficiencies. States of deficiency however, are very frequent and those wholly or partially due to deficiency, or mal-adjustment of quality or quantity of one or more factors obtained from food, are much more common than usually is appreciated. Ill health may be produced by deficiency of a food factor in much smaller amounts than necessary to create the typical syndrome associated with its lack. The effects of a persistent slightly faulty diet may become detectable only after many years and perhaps not for generations. The earlier evidences of disease from unsuitable food have been studied but little and demand the attention of clinicians.

All aspects of deficiencies cannot be discussed here. My remarks will be confined to a few concerning particularly nutritional deficiencies.

#### SOME HISTORICAL, PHILOSOPHICAL AND GENERALIZED ASPECTS

Descriptions were given of disorders due to excess and deficiency of internal secretions and to lack of vitamins long before there was recognition of these products from little chemical factories of marvelous ingenuity, and products capable of miraculous effects. Murray's discovery in 1891 that an extract of sheep's thyroid gland benefited patients with thyroid deficiency was one of the first to open up the field of endocrine therapy. The activities of John Huxham, of James Lind and Captain Cook in the eighteenth century in preventing scurvy pointed the way to the knowledge of today concerning the lack of vitamin C. In

referring to the influence of food for scurvy patients "to supply the elements wanting in their spongy tissues" Oliver Wendell Holmes<sup>13</sup> in a lecture given in 1861 made the following prophetic statements: "I have recognized that the perfection of art is often a return to nature and seen in this single instance the germ of innumerable beneficent future medical reforms." He continued: "I cannot help believing that medical curative treatment will by and by resolve itself in a great measure into modifications of food swallowed. The effects of milk and vegetable diet, of cod liver oil are only hints of what will be accomplished when we have learned to discover what organic elements are deficient or in excess in a case of chronic disease and the best way of correcting the abnormal condition." Cod liver oil was used for invalids in the eighteenth century. It was recorded in 1807 as of value in osteomalacia (Bardsley)<sup>14</sup> and in 1822 as a cure for rickets (Shutte), and yet it was about a century later before its therapeutic properties were truly comprehended. The importance of iodine and its therapeutic value in "goitre" was demonstrated in 1821 by Coindet and here again about one hundred years elapsed before the significance of iodine was appreciated. These remarks indicate how long it may take man to grasp the significance of observations. One must always be prepared to recognize that but a hair above the underbrush may mean that a large mammal is at hand.

Since the pioneer work of Eijkman (1897), Grijns (1901), Hopkins (1906) and Funk (1911) on vita-



mins, of Schiff (1859) and many others on internal secretions and of various investigators on the importance of inorganic elements, complete proteins and other substances in the diet, knowledge concerning these matters has progressed with startling rapidity. Even so, today's comprehension of a deficiency of many such substances, like the title of Holmes' lecture is but "Border Lines of Knowledge in Some Provinces of Medical Science" and is for revision tomorrow as progress will occur to upset today's erudition.

With the advent of new knowledge there is a tendency for the physician to attempt to apply it to a host of disorders. Undoubtedly many patients have received all sorts of glandular, vitamin, tissue extract and inorganic products which could not benefit them. Others that could be benefited by such products have had them prescribed in too small or too great amounts. This is partly because with the haste of modern life there is a tendency to avoid studying patients in a scholarly way, and to neglect the precise advice of qualified students. Furthermore the physician often does not have knowledge whether a given preparation has been proved to have potency. He is apt to be induced by the laxy to try new therapy, since the public has appropriated knowledge of vitamins, of other food elements and of glands of internal secretions before investigation has been concluded. Often these factors are considered the cause of all evils and there have arisen more or less rational ideas about them.

There is a growing danger in the tendency to attribute every nutritional

disorder to vitamins. One must remember that a well balanced adequate varied diet is of prime importance for health, a matter appreciated by the ancients and alluded to by such a pioneer as Lewis Cornaro, the Venetian who died in 1566, and whose book reached the fortieth English edition in 1821. Even if a patient's disease calls for a reduction of some type of food, the diet must contain at least a minimal requirement of all necessary elements. I have seen, as have others, improper dietary treatment lead to deficiency disorders, for example make patients with nephritis suffer from protein deficiency, those with duodenal ulcer develop scurvy, women with digestive symptoms become anemic from lack of iron in their food, and even beri-beri arise in a child fed by a physician's advice on three types of canned food.

Much of our knowledge concerning deficiencies, especially of vitamins, has been derived from experimental animals where one factor at a time can be varied. Although one often may interpret results obtained with animals as comparable to what may take place in man, the clinic must be the place where final knowledge concerning human beings is to be obtained. Deficiency diseases in man may have a complex etiology and dietary defects are often not alone the lack of vitamins, but complicated for example by incomplete or low protein intake, excess of carbohydrate, infection or by altered physiological mechanisms. Some of the outstanding disorders due to vitamin deficiencies in man are well recognized and have been studied critically. Clinical studies concerning nu-

trition comparable to those on animals are few and progress may be expected by the study of patients and the isolation by chemists of factors that in small amounts are so important for health. By carefully controlled and prolonged observations on patients one may expect to learn not only more about the clear cut deficiency diseases, but also much about conditions that represent abortive, incomplete or border line states of deficiencies. Probably many such conditions are not recognized but gradually will become so. Investigation will add knowledge about certain diseased states not due primarily to deficiencies but which can be in a measure prevented or alleviated by supplying the proper amount or balance of factors, which if incorrect can cause a nutritional deficiency disease.

Trained clinical investigators may help to unravel such problems as the influence of factors on the absorption or utilization of vitamins and the quantity of vitamins desirable to have stored in the body, but these matters among many others deserve scrutiny by every practitioner of medicine. A great deal may be learned from skillfully taken dietary histories, observations on habits and the influence of feeding given substances in large amounts for sufficient time.

#### PARTIAL DEFICIENCY

Diets are rarely selected by man so as to present the possibilities of clear cut dietary deficiency disorders as are encountered in experimental animals, but man undoubtedly often selects his food unwisely and obtains an undesirable diet that may lead to defects from

a prolonged consumption of a sub-optimal amount, or an improper balance of factors essential for health. It is disorders from long continued undesirable diets causing effects slowly over years or in a second generation that the clinician must watch for, rather than readily recognized defects from grossly abnormal diets taken over longer or shorter periods of time.

Confusion must not arise because deficiencies of two sorts occur in the same patient. We have observed the association of scurvy and true pernicious anemia, also of pellagra and pernicious anemia, the former being alleviated by a yeast concentrate and the latter some weeks later by potent liver extract. Furthermore a deficiency disorder due to food defects may occur in patients with a deficiency of an internal secretion and such cases offer matters for interesting speculation.

McCollum,<sup>30</sup> McCarrison<sup>27</sup> and others have pointed out how with the advance of civilization it is common to find people choosing diets composed of "ready to serve" or "grocery store" foods as those prepared by high heat, milling, canning, salting and the like, together with excesses of concentrated carbohydrate foods and sugar, with the omission of the so-called protective foods: fruits, vegetables, milk, and the organs of animals. Such diets obviously are undesirable and often do not contain optimal amounts of vitamins, and as McCarrison<sup>26, 28</sup> has suggested may be one reason why gastrointestinal disorders among highly civilized people are more frequent than among those living an aboriginal life. The rôle played by such diets in producing dental defects, decreasing re-

sistance to infection and inhibiting physical fitness and growth are recognized. Although disorders resulting from improper food may appear to be slight, under such circumstances they may slowly lead to altered functions or anatomical changes which permit organisms or other factors to be the more immediate cause of disease.

Deficiencies are more readily produced during growth, so one would expect to observe the effect of partial deficiencies more often in children than adults. Apparently in Europe and North America there is an increase of defective nutrition among children which can be attributed sometimes to the mother's diet and in other instances to the child's. McCollum<sup>20</sup> and Mellanby<sup>21</sup> have emphasized this and suggested that many border line cases of malnutrition are due to sub-optimal amounts of particular substances. Hoobler<sup>19</sup> has given evidence that it is not uncommon for pale and undeveloped, fretful infants with anorexia and spastic muscles to suffer from partial vitamin B deficiency, a condition readily alleviated by the ingestion of "yeast vitamin B concentrate." The rôle that vitamin B plays in stimulating the appetite sense, as first shown in dogs by Karr<sup>22</sup> and later Cowgill<sup>23</sup> is for clinical consideration and many observations should be made concerning the part played by this factor, or some part of it, in the nutrition of the nervous system. It is to be recalled that every sort of nervous disorder is more common among civilized than non-civilized people, and although there are many reasons for this one may wonder what rôle, if

any, is played by inadequate diet and lack of specific dietary factors.

Oftentimes it is not simple to elicit from the patient that his diet has been a defective one—a matter emphasized by that illustrious student of pellagra, the late Dr. Joseph Goldberger, who did much to aid mankind and whose studies demonstrated that lack of the —P P— factor of vitamin B causes pellagra. In response to casual questions the patient is apt to reply, for example, "Yes, I eat meat and green vegetables," but upon careful questioning the amount will be found to be trivial or the form peculiar. Furthermore one must recognize that individual constitutions, with known or unknown defects, may explain why one person readily develops a deficiency disorder on a given diet and another does not. A condition favoring the development of a deficiency disorder may be obvious, for example partial intestinal obstruction may permit pellagra to develop easily and pernicious anemia has been associated with the same cause. Likewise chronic alcoholism favors the development of pellagra and some other deficiencies. The rôle that the gastric achlorhydria induced by alcohol may play in the development of such conditions is referred to further on.

#### ILLUSTRATIVE CASES OF PARTIAL DEFICIENCY

Two examples are cited below to illustrate further the nature of border line cases of deficiency disease or partial deficiencies arising in adults.

A woman, 45 years old, who has always lived in Massachusetts had experienced for 15 years symptoms of

colonic indigestion. On reflection the case may appear simple to diagnose, but as she had consulted a large number of physicians without obtaining the diagnosis I offer, or without relief it is evident that the condition is not well understood. In spite of trying 'all sorts of diets' her gastro-intestinal symptoms continued and increased, though they were less when she was forced to take a little steak. Gradually she lost weight and muscular weakness became prominent. A secondary anemia with hemoglobin 60 per cent developed. Leading questions brought forth the fact that in May, two years before she was seen, she had "an insignificant generalized eruption on the back of her hands from her wrists to her knuckles that later peeled" and that this recurred to a trivial degree a year later. This area of her skin appeared slightly more pigmented than her finger tips or arms. All sorts of tests yielded no further significant information except that she had achlorhydria. At first she described her diet in such a way as to suggest that it was satisfactory, but it was soon learned that although there was set before her a nutritious diet she had always been fussy and particular about her food. In spite of special diets and having eaten a little of many sorts of food, for years she had eaten much dextrinated food, many French and English biscuits prepared for invalids. For years meat had been eaten scantily and only when cooked for an unduly long time, while fruits and green vegetables had been taken in never more than minimal amounts particularly in pureed form without cream. The patient was fed daily for

two weeks no other food than 225 grams of calves' liver—a food rich in many elements including the P P factor, a component of vitamin B—; one orange and 70 grams of bread. With startling rapidity all her symptoms of many years' duration vanished, and now for two years she has been on an ordinary well balanced diet and remained in complete health. This case illustrates a form of pellagra where the defective diet led particularly to gastro-intestinal symptoms and only after years permitted the appearance of the mild skin lesions.

Patients with pernicious anemia often have gastro-intestinal, as well as at times central nervous system symptoms, long before there is evidence of anemia, and it is then that they should receive liver treatment rather than when anemia becomes pronounced. Cases of this sort may be considered border line ones of a deficiency disorder. A clear cut example is the case of a man whose two older brothers have pernicious anemia. His blood repeatedly showed no signs of anemia, but achylia gastrica was present. For years he suffered from intestinal symptoms and often for weeks at a time would have from one to three stools a day. Muscular weakness and vascular hypotension were features as were ill defined "neuritic" pains in different parts of his body. There were however no symptoms confined to the hands or feet or referable to disease of the central nervous system. For a month he was fed a diet rich in muscle meat without improvement. Then for a month he took a normal diet with large amounts of both wheat germ oil and a yeast con-

centrate, thus supplying him with large amounts of both parts of vitamin B (vitamin F and G). On this regime he became perhaps slightly better. In the third month he continued with the same diet and took large amounts of a liver extract rich in the substance effective for pernicious anemia. Within the month his whole sense of well being improved extraordinary and his gastro-intestinal symptoms vanished. He has continued for 18 months to take liver extract and a normal diet and his symptoms have not returned. Not only are there probably comparable cases to be alleviated, but many individuals with similar symptoms, who can be benefited by following out the prescription of an adequate well balanced diet — for example many young women eating "soda fountain counter lunches" and obtaining a hastily swallowed scant breakfast, who suffer from slight simple anemia and gastro-intestinal symptoms.

#### DEFICIENCY FROM INADEQUATE UTILIZATION OF SUBSTANCES AFTER THEIR INGESTION

An individual may ingest a sufficient amount of material to prevent a dietary deficiency disorder, but in spite of this the disorder may develop if his organs are unable to utilize or prepare the necessary substance. That adequate amounts of absorbed vitamin are made available to the body is suggested by Kerner and Williams<sup>22</sup> among other persons. Their studies suggest that vitamin D, even in large amounts, cannot prevent the development of rickets in certain rats. Perhaps the same is true of other vitamins.

sclerosis may act to precipitate symptoms of deficiency in the presence of an amount of active principle sufficient in health for the avoidance of symptoms. Damage to the blood vessels could prevent cells from obtaining readily a suitable supply of an active principle. Observations by Dr Weiss and myself suggest that an abnormal condition of the vascular system may be one that favors the development of scurvy in adults and hinders the effect of the substance effective in pernicious anemia.

Impaired digestion may prevent the proper absorption or assimilation of vitamins. Probably deleterious effects from taking below optimal amounts of vitamin B and C are enhanced by lack of absorption or the influence of intestinal bacteria, when the food is improperly balanced, especially when associated with an excess of carbohydrate. The antagonistic action of something in certain fats and oils which counteracts the curative effect in animals of vitamin E is noted by Evans and Burr;<sup>10</sup> and Mattill<sup>24</sup> has observed that oxidative changes within the intestine can decrease the potency of given amounts of vitamin A. Ferrous sulphate<sup>9</sup> also can act to destroy vitamin A. On the other hand there are factors that can favor the action of a vitamin. Sunlight can do this. Evans and Lepkovsky<sup>11</sup> have noted that it takes less vitamin B to protect animals when fat is present in the diet than when it is not; and there are other observations to suggest that certain combinations of substances enhance vitamin activity. Other facts are available to indicate the importance of supplying a lacking substance with a

well balanced diet containing nothing to hinder and perhaps something to favor its action.

### THE ROLE OF ACHYLIA GASTRICA

Inability actually to obtain or digest from food a substance necessary in small amounts for the maintenance of health has been demonstrated by Castle. His work in an epoch making contribution to human gastric physiology and towards the understanding of the disease pernicious anemia, in which gastric achlorhydria even following the injection of histamine practically always occurs long before and after treatment Castle has shown conclusively that whereas the daily feeding of 200 grams of beef steak produces no effect on the pernicious anemia patient, this amount of beef steak when digested for about an hour in either a normal stomach or in vitro with normal gastric juice and then fed daily to the patient produces effects entirely like those seen with liver therapy. On the contrary no benefit occurs from the feeding of beef steak digested with only commercial pepsin and hydrochloric acid. This work clearly indicates why achylia gastrica can play an important rôle in the development of pernicious anemia.

The frequent occurrence of gastric achlorhydria in various deficiencies tempts speculation concerning its influence. There are few observations as to whether or not achlorhydria, if present, persists after histamine injection in other deficiencies than pernicious anemia and this matter is worthy of study. Undoubtedly in many cases achlorhydria develops as the result of

a deficiency, but in pernicious anemia it occurs before obvious signs of the disease appear and it may in other sorts of deficiencies play an etiological role. Achlorhydria in scurvy of adults is common, but free acid often returns as the patient gets well. In myxedema, hypopituitarism, diabetes mellitus and Addison's disease achlorhydria is not uncommon. It is found with great frequency in pellagra and often persists after the patient's symptoms are alleviated. The condition occurs in beri-beri and has been reported to develop sometimes in animals fed diets deficient in vitamin B.

It is recognized that chronic alcoholic patients develop gastric achlorhydria and are potential pellagrins, as they appear more susceptible to pellagra following an insufficient diet than those who are not addicted to alcohol. It seems that pernicious anemia also may be aided to develop by chronic alcoholism. Cases of peripheral neuritis, yet not considered beri-beri, associated with vitamin B deficiency have been reported<sup>23</sup> and gastric achlorhydria may accompany multiple neuritis. Dr. Castle and I have noted that the two diabetics we have observed recently with peripheral neuritis had achylia gastrica and their symptoms slowly improved upon taking large amounts of a concentrate of yeast. With these facts in mind and the recognition that vitamin B deficiency leads to disorders of the nervous system one must wonder if achylia gastrica is not a factor that can inhibit the utilization of both the P P and anti-neuritic factor of vitamin B. It may be recalled for data upon which to build hypotheses that the pathologi-

cal changes in the spinal cord in pellagra may simulate entirely those found in pernicious anemia. The work of Boyenval<sup>3</sup> and Koskowski<sup>21</sup> on animals is also of interest in this connection. They have shown that if rats are fed vitamin B deficient diets and given injections of histamine that they do not develop the premortal nervous disturbances observed in control animals. These thoughts and facts suggest that an elucidation may be arrived at from carefully made and controlled clinical observations upon patients with gastric achlorhydria and symptoms even of a trivial sort referable to the nervous system.

#### THE ROLE OF BALANCE BETWEEN VITAMINS AND OTHER SUBSTANCES

The balance of factors or the relative proportion of each is often a more important aspect of biological mechanisms than the presence of an absolute amount of a given substance. The interrelationship of the glands of internal secretion and the influence of some of their secretions upon metabolites is recognized. There is little knowledge concerning the importance of vitamin balance and the effect vitamins have on inorganic metabolites or vice versa, upon hormones and so forth. Such matters can be studied in the clinic while progress is made in the laboratory. Burrows<sup>4</sup> has suggested that when vitamin A predominates over vitamin B the growth of rats is delayed and hastened under opposite circumstances. The effects of a diet rich in vitamin B are difficult to observe when vitamin B are deficient, but are worthy

of study. Perhaps the recognized influence of vitamin A to increase resistance to infection is enhanced when its balance with vitamin B is of a given sort. In such a condition as chronic hypertrophic (osteo) arthritis one may wonder what rôle, if any, is played by vitamin balance within the body. In such a consideration one should recollect that metabolic changes, or those due to infection or altered digestion, could be in themselves but the expression of a disorder favored by an unsuitable soil existing for years dependent upon the consumption of food factors in non-optimal quantities. One may ask is it possible that in man the genesis of certain urinary calculi can be attributed to an imbalance between vitamins and organic metabolites, which is suggested because vitamin A deficiency in rats, as Osborne and Mendel<sup>11</sup> first noted in 1917, induces the development of calculi, but marked vitamin A deficiency is rare in man.

The effect of vitamin D upon the metabolism of calcium is classic and it is probable there are various other comparable mechanisms in the body. In fact, McCarrison<sup>26</sup> has hinted at a relationship between manganese metabolism and the vitamins. Under certain circumstances the feeding of liver and iron can produce a greater effect on blood formation than either alone. Hart and his associates<sup>16</sup> have shown that copper enhances the action of iron in the formation of hemoglobin in rats rendered anemic by a milk diet and copper can be a catalyzer of value in avitaminosis<sup>9</sup>. The supplementary effect of one substance upon another is undoubtedly an important one to not lose sight of. There is

probably, at least under certain circumstances, an important quantitative relation of vitamin B to protein intake as shown by Hartwell's<sup>11</sup> studies on the mammary secretion of rats

It is possible that there is some optimal balance between some vitamins and some hormones. However, it is known that vitamin deficiency can affect glands of internal secretion, for example, it is recorded that lack of vitamin B increases the size of the islands of Langerhans<sup>1</sup> and hypertrophy of the suprarenals.<sup>12</sup> It is also stated<sup>12</sup> that vitamin B may decrease the blood sugar in diabetes mellitus. Changes in the thyroid gland can result from vitamin deficient diets in the presence of sufficient iodine.<sup>9, 13</sup> The complexity of the many possible interrelations of substances, the lack of which lead to a deficiency disorder, has been alluded to, simply to indicate the desirability of thinking broadly, and to recognize there are many reasons for therapeutic results and many ways they may be brought about.

#### INFECTION IN DEFICIENCY DISORDERS

Infections can intensify and precipitate the symptoms of a deficiency disorder which is important for the clinician to appreciate. Their effect is one of other illustrations concerning the similarity of behavior between vitamins and hormones. Mild, often temporary, states of hypothyroidism and decreased function of other glands of internal secretion occur following infectious disease, such as influenza, pneumonia and typhoid fever. Infections may be responsible for pronounced dysfunction of the glands of internal secretion. Vitamin deficiency

disorders too, may be precipitated in the wake of an infection. This serves to stress the importance for individuals to maintain in their body optimal amounts of the necessary accessory food factors.

Infections arising in the diabetic are well known to lower his sugar tolerance. In myxedema patients, also, infections apparently intensify their deficiency. It is a striking fact that infections in untreated cases of pernicious anemia hinder the beneficial influence of liver. They are the chief cause of significant decreases of the red blood cells in such patients with normal red blood cell counts taking with regularity reasonable amounts of liver. Thus, in the presence of infection in these three conditions when the patients have been maintained in satisfactory health, it is often necessary in order to prevent progressive signs of deficiency to prescribe an increased amount of active principle. Likewise, when treatment is begun it will require the administration of larger amounts of active principle to obtain the best possible results than are necessary when infection is absent. A similar state of affairs apparently holds true for pellagra and probably for at least some other deficiency disorders. The exact mechanism of the effect of infection upon patients with deficiencies, but maintained in health by the daily administration of specific substances is yet to be explained. In seeking an explanation it is worth noting that there is some similarity in the chemical nature of the specific substances involved. The products are nitrogenous. The part of vitamin B that has been isolated, and, in all prob-



ability, the part that has not been isolated and the substance effective in pernicious anemia, which has basic properties, are small in size, as are thyroxin and adrenalin. The two latter are known to be relatively simple compounds related to the amino acids of food protein and probably derived from them. Insulin, like secretin is larger in size and a polypeptid

#### TREATMENT WITH OPTIMAL DOSIS

It is a first principle of therapeutics to administer enough of a substance to obtain an optimal effect and to not be satisfied with improvement unless it is as great as possible. Untoward symptoms from excessive dosage are to be avoided. There is little knowledge about the effects of large doses or a long continued excessive intake of vitamins. It is known that too much irradiated ergosterol (vitamin D<sup>2</sup>), can soon lead to deleterious results and excess of anti-pernicious anemia substance in patients with this disease cause undesirably high levels of the red blood corpuscles. The dosage of some substances, the lack of which leads to a deficiency disorder is well understood, but little is known about others. Remarkably small amounts of products from nature's little chemical factories can do much good. It is evident, however, that the minimal daily quantity required by a normal person to protect him from deficiency is often much less than the optimal quantity for health or the amount required to alleviate satisfactorily a patient with a deficiency disorder. In trying out new therapeutic procedures this should be borne in mind and also the principle of giving enough for a long time, even if

in the form prescribed it seems excessive. Such treatment may lead to important results where failure appears from too small amounts. Our results with the liver treatment of pernicious anemia illustrate this.<sup>21</sup> The daily ingestion of 75 grams of liver will accomplish little and in some cases produce no effect, whereas 225 or more grams will cause rapid improvement. Blumgart<sup>2</sup> has studied in detail a woman with severe osteomalacia who showed no improvement at all after taking daily for 18 months about 20 grams of cod liver oil of high vitamin D potency. Her diet apparently contained at least an amount of calcium suitable for a normal woman. When she was given daily five times this amount of vitamin D and 20 grams of calcium, rapid progressive improvement took place which was hastened by the application of ultraviolet light. The clinical and roentgen-ray observations demonstrated that ossification of the bones had occurred. The patient is now well. The case points out again, as does the following example, the importance of adequate treatment. There is literature to the effect that large doses of iron can be effective where commonly prescribed doses are inert. Some recent observations made with several of my associates indicate that although the normal body requires but about 15 milligrams of iron a day, distinct rapid effects are produced in certain cases of chronic secondary anemia, particularly those of obscure or dietary origin, when 350 milligrams of iron are fed yet insignificant or negative results may be obtained when 50 milligrams are ingested.



The importance of an adequate varied diet for man with optimal amounts of all necessary factors

Many types of deficiencies may occur in man and dietary deficiencies are of numerous kinds

The probability that sub-optimal amounts and balances of vitamins, minerals, amino acids and so forth taken over long periods of time favor ill health and incomplete growth and decrease physical fitness and the chances for longevity

Lesser grades of deficiency disorders exist that are often unrecognized and may appear only after years of an undesirable diet

Many factors, as infection, may operate to produce or intensify symptoms from a deficiency

Improper diet may not be the cause of a deficiency arising from lack of material contained in food, because the individual may be unable to prepare or assimilate a required factor

One should not think of vitamins, or substances the lack of which produce symptoms of deficiency, as

causing only a particular disease or a special symptom but consider what tissues or functions they affect. Each plays its own rôle in the body's economics and tends to affect definitely certain types of cells or functions as is well illustrated by Wolbach's studies

The proper treatment of deficiencies necessitates recognition that there is a quantitative relationship, up to a maximum, between the amount of substance the patient receives and the degree of benefit that he will obtain

Vitamins and hormones and the lack or excess of other chemical substances are not the cause, nor will they cure, all evils. In time one will reflect that today's erudition concerning these substances was but "border lines of knowledge"

The laboratory does not supply something absolute, it increases the necessity for careful clinical study. In doing so, treatment with a sufficient amount of material is important for success. Final knowledge regarding deficiencies in man will be obtained by studying with adequate controls *homo sapiens*

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# Some Physiological and Biochemical Aspects of Deficiencies with Special Reference to Vitamin B\*

By GEORGE R. COWGILL, *New Haven, Conn*

MUCH of the support for the vitamin hypothesis has come from the experimental laboratory of students of nutrition. The pioneer work in this field, however, had a clinical origin centering around the disease beri-beri. In his monographic study of this disorder Vedder (1913) championed the idea that the primary etiological factor is lack of a vitamin substance. Many clinicians, however, especially among the Japanese (Ogato et al, 1923) hesitate to concur in this opinion, because experimental beri-beri in animals differs in certain respects from human beri-beri as seen in the clinic. Whereas the experimentally produced condition may be due to lack of one dietary essential, the case observed by the clinician is more likely to be the result of a multiple rather than a single deficiency. Consider "wet" and "dry" beri-beri (figure 1).

Each is characterized by the same neuromuscular symptoms. How may one explain the presence or absence of

edema? Studies of edema indicate that this condition is associated with a low concentration of blood plasma proteins. By feeding diets low in protein for extended periods, edema has been produced experimentally (Harden and Zilva, 1918, Kohman, 1920). It is conceivable that cases of "wet" beri-beri are suffering not only from a deficiency of a particular vitamin but from a shortage of protein as well. The syndrome illustrated in figure 2 (Cowgill, 1921) is readily produced in dogs by feeding the animals with an artificial food mixture rich in protein and other dietary essentials but deficient in the antineuritic vitamin.

The condition of this dog is quite similar to that of "dry" beri-beri shown in figure 1. In this experimentally produced condition edema has never been observed, so far as known these animals lack only one dietary essential, namely the antineuritic vitamin.

The ideas advanced concerning the rôle of the individual vitamins reveal a variety of viewpoints, some attributing a general type of function involving every cell, others suggesting a more specific part in relation to certain organs or systems of organs. Vitamins have been conceived as indis-

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FIG. 1. (Left) Subject in the position of the patient. (Right) Subject in the position of the observer.



pensable (1) for the metabolism of carbohydrate, protein, fat, lipid substances and the like, (2) for the mechanisms of biochemical oxidations and reductions, (3) for immunity reactions, and (4) for the metabolism of cell nuclei. According to Dutcher (1920) the body's hormone supply may be dependent upon the vitamin content of food. This very brief summary indicates in some measure at least how broad a field the study of vitamin physiology has come to be.

It is obvious that in the short time available, one cannot give any detailed and complete review of the many deficiency conditions now recognized. A survey of the literature indicates vitamin B to have initiated more diverse lines of investigation and theorizing in regard to its function than is the case with any other member of the vitamin group. For this reason, and because of the interest which these different types of investigation possess, this dietary factor has been selected as a focus for the present discussion.

### VITAMIN B

What has hitherto been called vitamin B has quite recently been shown

to consist of at least two physiologically active substances—one destroyed at high temperatures and effective in preventing and curing the neuritic symptoms of experimental beriberi, the other component stable toward heat, required along with the anti-neuritic factor in promoting growth, and probably effective in curing and preventing the development of pellagra. Many workers have called this second factor the "growth-promoting" fraction of vitamin B. This is incorrect for experiment has shown that growth can occur only when both of these factors are present (see Smith, 1928).

Continued subsistence on a diet adequate except for vitamin B eventually leads to a partial or complete anorexia for the experimental ration. In the illustrative chart—figure 3—the maximum black ordinate column represents the amount of the vitamin deficient ration offered daily to the animal. The heights of the columns from day to day indicate the amount of the ration voluntarily consumed by the dog. It will be noticed that this animal—dog 39—developed anorexia

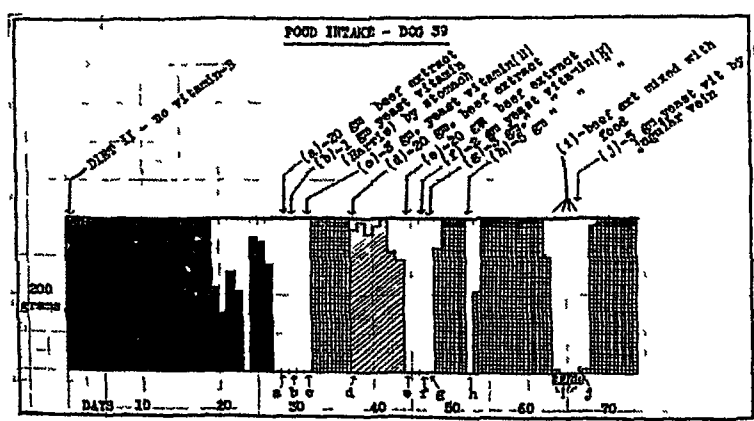


FIG 3 (From Cowgill, Denel and Guidle, 1925)





der the symptoms more severe. Random and Simonnet (1924) quite recently reemphasize this view. However, the variation in time of onset and severity of symptoms which groups of experimental animals show, is in our opinion so wide that one may seriously question any hypothesis resting largely on such evidence. The failure of Osborne and Mendel (1922) and Sherman and Gloy (1927) to observe any differences in vitamin B requirement of animals subsisting on diets having extremely unusual proportions of organic nutrients has been cited as evidence against this theory. Evans and Lepkovsky (1928) have just reported that fat in the diet spares vitamin B. A definite amount of the B factor in the form of yeast was insufficient for rats subsisting on a diet extremely rich in protein. When the ration was changed to include a fairly large proportion of fat, this same amount of vitamin B now proved adequate. Studies of the respiratory quotient in this deficiency have yielded conflicting results.

The old idea that toxins are responsible for the neuritic symptoms of vitamin B deficiency was considered

incompatible with the vitamin theory and rightly so because the toxins were regarded as existing preformed in the food. A later suggestion is that the hypothetical toxins may be abnormal intermediary metabolites arising in the course of faulty carbohydrate metabolism because of absence of the vitamin factor (Walshe, 1918). The almost miraculous recoveries from the severe neuromuscular symptoms of advanced vitamin B deficiency that animals show when given the missing factor are difficult to explain on the basis of mere neutralization of toxins by the vitamin (Figure 5). Dogs exhibiting clonic spasms, when handled, have been given complete relief within as short a period as four hours by intravenous injection of a suitable vitamin B concentrate (Cowgill, 1923) (Figure 7). This is comparable to the well-known remarkable recoveries that pigeons make in similar experiments (Funk, 1914).

Attempts to show that vitamin B plays a rôle in the mechanisms of tissue oxidations and reductions have yielded diametrically opposite results (Abderhalden and Weirtheimer, 1921; Drummond and Maitlan, 1926).



FIG 5 DEFICIENCY OF ANTINEURITIC VITAMIN B. ADVANCED CASE (Funk)  
Before treatment and 3 hours after receiving 4 mg of yeast vitamin concentrate parenterally

The decrease in the basal metabolic rate of animals restricted to a diet lacking vitamin B has been emphasized by many writers with the implication that the vitamin-lack exerts a peculiar specific effect on the basal rate. Most of the observations have been made on pigeons subsisting on a diet of white rice. Such a ration is deficient in several respects. Deuel and Weiss (1924),

however, using the animal calorimeter at Cornell Medical College, made direct measurements on dogs subsisting on diets similar to that fed the animal shown in figures 6 and 7. The observed lowering of the basal metabolic rate was believed to be entirely accounted for by the accompanying partial starvation resulting from the anorexia induced by the vitamin de-



FIG 6 DEFICIENCY OF ANTINEURITIC VITAMIN B ADVANCED CASE (Cowgill)  
*Before treatment* Contracture of leg muscles Clonic spasms when handled  
*18 hours after receiving tomato juice via stomach tube* "Steppage" gait

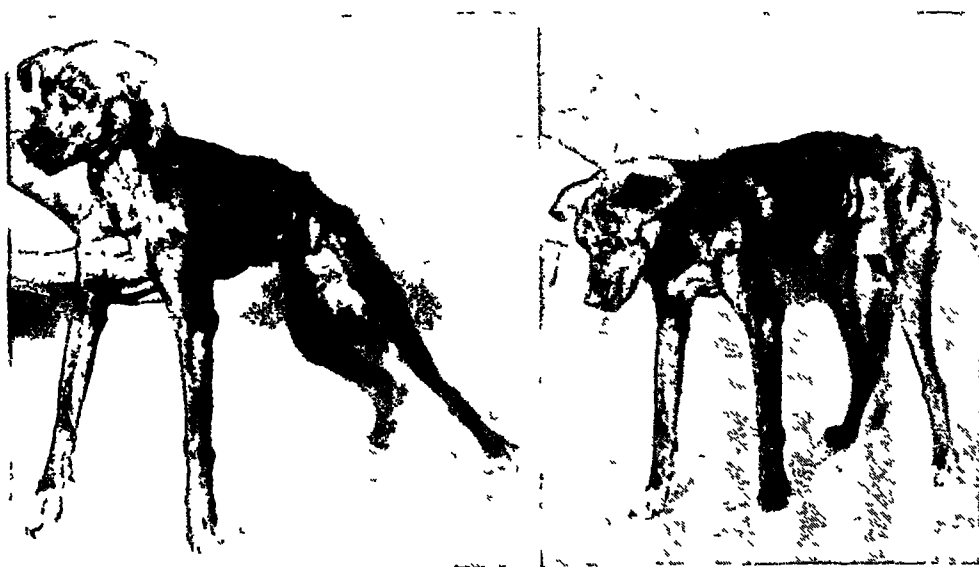


FIG 7 DEFICIENCY OF ANTINEURITIC VITAMIN B ADVANCED CASE (Cowgill)  
*Before treatment and 4 hours after receiving vitamin B extract intravenously* dog is now able to walk but with a slight spasticity of the hind limbs

iciency Lusk concurred in this opinion

Vitamin B has also been regarded as a specific stimulant of digestive glands like the drug pilocarpine for example (Uhlmann, 1918) We have failed utterly to confirm this experimentally (Cowgill and Mendel, 1921) The anorexia characteristic of lack of this dietary essential suggests a disturbance of gastric motility, perhaps a disappearance of the so-called hunger contractions We have studied this problem in dogs (Cowgill, Deuel, Plummei and Messer, 1926) Only minor changes occur in the motility of the empty stomach during the early stages of vitamin B deficiency and these are insufficient to account for the anorexia Gastric atony is almost invariably part of the syndrome of an advanced case of this deficiency

This conclusion has been questioned (Smith, 1927) but a renewed and more extended investigation in our laboratory has only served to confirm our earlier findings (Stucky, Rose and Cowgill, 1928) Some evidence has been offered suggesting that the processes of gastric secretion are depressed in this deficiency (Farnum, 1926), also that the motility of the intestine is impaired (Plummei, 1927) We are of the opinion that the gastro-intestinal features of this deficiency are not the result of a peculiar specific relation of this vitamin to functions of the organs of the alimentary canal, but rather are reflections of a deranged systemic condition

The view that the antineuritic vitamin B plays a rôle in the metabolism of cell nuclei and is therefore a substance required by nearly all cells of

the body has much to commend it (McCarrison, 1919, Findlay, 1921) Various tissues appear to rank in content of this vitamin according to their richness in cell nuclei, liver, kidney, brain in contrast to muscle for example Furthermore the numerous attempts of biochemists to isolate this vitamin suggest that it is a substance closely related to well-known constituents of nucleic acid (see Krause and McCollum, 1929) Recent quantitative studies made in our laboratory of the vitamin B requirements of different size individuals of several species find a reasonable interpretation in terms of this hypothesis If it may be assumed that deficiency of the antineuritic vitamin B is a species of nuclear starvation in which the heart and central nervous system are spared as long as possible at the expense of other organs, then the pathologic, physiologic and metabolic findings seem to harmonize fairly well It is unnecessary to postulate, as Cramer (1923) has done, a special rôle for vitamin B in the functioning of lymphoid tissue, a tissue rich in cell nuclei, be it remembered To do so is to emphasize but a single detail of the picture

#### VITAMIN A

The exact chemical nature of this dietary essential is still unknown Takahashi's (1924) claim to have isolated this vitamin has been disputed by Drummond, Channon and Coward (1925) The data submitted by all of these investigators suggest that vitamin A is a complex unsaturated higher alcohol or a closely allied substance

This dietary factor is required for growth Shortage of vitamin A dur-

ing the early stages of development may have a deleterious effect for long periods (Sherman and Burtis, 1928) Translating the studies on rats to the



FIG 8 VITAMIN A AND GROWTH

Two rats of same age, fed same ration except that the rat on *right* received Vit A in addition (McCollum)

human species Sherman and Burtis estimate that inadequate supply of vitamin A to an infant during the first two years of life may predispose that child to infections, pulmonary disorders and the like for the following eight or ten years. This vitamin is also required for maintenance of the adult, and inadequacies of supply adversely affect longevity (Sherman and Macleod, 1925)

A characteristic eye disease develops in vitamin A deficiency. This

has been observed in experimental animals and in human infants (Osborne and Mendel, 1921, Steenbock, Nelson and Hart, 1921, Bloch, 1924)

According to Wolbach and Howe (1925), the pathological change of note is a keratinization of epithelial tissues. The infections occurring, when vitamin A is lacking, are probably of secondary origin resulting conceivably from an impairment of the cells of the protective surfaces involved. Opsonins are not decreased in



FIG 9 OPHTHALMIA IN DOG—VITAMIN A DEFICIENCY

*Left* before treatment *Right* cured in ten days by addition to diet of 20 cc of cod-liver oil daily

(Steenbock, Nelson and Hart)

this deficiency (Findlay and Mackenzie, 1922).

It is conceivable that vitamin A plays an essential rôle in lipid metabolism, or that it is a necessary constituent of the lipoidal membrane of cells, that in its absence, permeability of that membrane is impaired, and the cell's capacity for absorbing nutrients or discharging secretion through that membrane is lowered or destroyed. Attempts to construct anything like a detailed hypothesis concerning vitamin A function must, in view of the present state of knowledge, involve considerable speculation.

### VITAMIN D

When evidence was obtained suggesting that a fat-soluble organic factor plays a rôle in preventing and curing rickets, vitamin A was thought to



FIG 10 Terrier with rickets (Mellanby)

be that substance (Mellanby, 1919). McCollum and associates (1925) succeeded in demonstrating that the antirachitic factor is separate and distinct

from vitamin A. From the recent work of Hess, Windaus (1927), Rosenheim and Webster (1926), it appears highly probable that the antirachitic factor is a derivative of ergosterol produced by exposure of this substance to radiant energy of wavelengths found in the ultra-violet zone.

The well-known facts concerning the rôle of this substance in the etiology and cure of rickets need not be reviewed here. Interesting problems now commanding attention concern the mechanism by which this factor exerts its influence on calcium and phosphorus metabolism, and its possible relation to the parathyroid hormone. Injections of irradiated ergosterol into normal animals can increase the level of blood calcium even when this element is absent from the intestinal lumen (Hess, Weinstock and Rivkin, 1928). Evidently such a rise in blood calcium cannot be attributed to increased absorption of lime from the alimentary canal. Administration of irradiated ergosterol to parathyroid-ectomized individuals does not produce a rise in blood calcium. Whereas the fresh egg contains large amounts of the antirachitic factor, the tissues of the newly hatched chick are devoid of it. Fish eggs and fresh fry exhibit the same phenomenon (Hess, 1929). Evidently, like vitamin B, the antirachitic factor is consumed in metabolism and the supply must therefore be renewed through the medium of food or exposure of the organism to radiant energy of the proper wavelength. Such exposure produces synthesis of this factor within the organism itself.

## VITAMIN C

The water-soluble factor required in order to prevent scurvy in man, monkey and guinea pig, is a substance very sensitive to oxidation, and apparently of molecular complexity comparable to that of a six-carbon-atom sugar (Connell and Zilva, 1924). Its exact chemical nature is as yet unknown. Apparently this substance plays an important rôle in the matrix of connective tissue. What the details of that rôle may be, one can only speculate upon. Not all species require this factor in the food. Scurvy has never been produced in the dog, rat or chicken. The most acceptable explanation of this fact at the present time seems to be that these species have the power of synthesizing vitamin C.

## VITAMIN E

In vitamin E deficiency the characteristic phenomenon observed in the female is *fetal death and absorption*. In the rat, whose gestation period is twenty-one days, this occurs at some time between the twelfth and the twentieth day of gestation (Evans, 1925). In the male, lack of this factor results after a time in destruction of the germ cells and eventually the entire seminiferous epithelium (Mason, 1926). In the case of the female there is no degeneration of germ cells, the ovary and ovulation continue unimpaired throughout life.

The chemical structure of vitamin E still remains unelucidated in spite of much research. This substance is remarkably stable toward heat, light, air and many of the ordinary chemical reactions. The viscous oil obtained

by Evans and associates (1925) "contains only a trace of ash, and no nitrogen, sulphur, phosphorus or halogen". Apparently it is a saturated compound in contrast to the other fat-soluble vitamins A and D.

Studies of these many deficiencies give new content to the idea expressed in the term *diathesis*. What seems to be a constitutional predisposition toward certain disease conditions may after all be the response of the organism to a deficient diet.

There has developed a tendency on the part of investigators generally to interpret all unexplained nutritional phenomena in terms of the vitamin theory. The pendulum of interest must not be allowed to swing too far away from consideration of calories, proteins and mineral nutrients, still necessary components of an adequate diet. Also one must not forget the need for a proper balance of the essential constituents of the diet already known.

A vitamin may be regarded as any substance (1) required by the body, (2) consumed in metabolic processes, and (3) necessarily provided from without because it cannot be synthesized within the organism except, as in the case of vitamin D, under special conditions. It is not unreasonable to suppose that additions will be made to the list of vitamins. The great complexity of the animal body, the variety of chemical compounds found therein, and the possibilities and limitations of the organism with respect to the processes of intermediary metabolism all afford an adequate basis for this belief.

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# The Treatment of Angina Pectoris\*

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**A**NGINA pectoris is not a disease, but a symptom complex. It has a widely varied etiological pathology which produces, nonetheless, a symptomatic picture of very striking and significant character, best as first described by Heberden in 1768.

The pathology, basically concerned is the cause of death in angina pectoris. All or any of these lesions may exist without the appearance of the symptom complex and the pathological changes are in themselves probably quite as likely to cause sudden or ultimate death without angina as with it. The symptoms of angina in themselves are not lethal, they may probably exist or at least be very closely simulated without any danger of sudden death. Symptoms are only dangerous when associated with or incited by the basic pathology of the condition.

The pathology of true or sinister angina pectoris is disease of the coronary arteries, aortitis, myocarditis or myocardial degeneration. In some instances pericarditis about the cardiac base may also so act, but it is also then commonly associated with disease of the heart muscle.

Relief or cure of the basic lesions, cures and eliminates the complex. Relief or cure of the symptoms does not

either remove the disease or materially alter its dangers. The symptoms are produced by a sensitized nervous arc, having its basis in stimuli which originate from the primary cardiac disease. Breaking of this arc, as, for example, by sympathectomy may entirely relieve the symptoms, but it has little or no influence on the basic pathology or on the inherent danger to life.

The speaker feels that the recognition of these axioms is essential for a proper and adequate understanding of the treatment of angina pectoris.

It has been noted that the basic pathology of angina pectoris consists exclusively of cardiovascular lesions. The dominant hereditary influence existent in most diseases of this character is apparent to every thoughtful practitioner.

Every one of us can call to mind families in his clientele which are particularly prone to arteriosclerotic disease, to hypertension, to cardiac fibrosis, to death from cerebral vascular insult, and most of us know also families in which angina pectoris is so frequent an occurrence as to correctly justify the appellation of Anginal Families.

Such being the case, the speaker feels that much can and should be done in the way of prophylactic treatment in such families so that this

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group tendency is eliminated or minimized

Families which show a tendency in this direction associated with obesity, for example, may largely lessen this trend by careful study and control of the dietetic and physical activities of its younger members. We must of course recognize that we can not entirely control these tendencies, for many of them are founded on endocrine dyscrasias, still even these influences may be to some extent controlled or prevented in early youth by study and treatment directed to the thyroid, pituitary and perhaps to the sexual glands.

Physical exercise control is a very important matter in the development of the youths of such families. Much danger lies in over exercise and in the cultivation of cardiac hypertrophy, arterial tension, and the like, from over physical exertion in early life. The youth of an anginal family should not undertake football, the crew, or the long distance run in his school and college years. On the other hand adequate physical exercise beginning in early life and continuing in temperance into the adult period is to be encouraged and directed. Excesses must never be permitted. Walking, golf, swimming, horseback riding and the like never in excess, are always beneficial, unless inherent heart defects are known to exist.

In the anginal family the youth should be taught self-control, not only of his physical expression but of his mental and emotional life also, for we all recognize the tremendous rôle which emotional stresses play in the evolution of angina. A very impor-

tant matter in the prophylactic treatment of angina is the development during youth, of diversions, avocations, hobbies and the like which lead to emotional rest and relaxation. Habits of healthful and adequate sleep must be also developed.

The infections, many of the juvenile types, which we all too frequently ignore, should receive more than ordinary attention in families which manifest this tendency. Temperance in all things, particularly in the use of alcohol, tobacco and of the condiments in general should be engendered.

Such infections as rheumatism, tonsillitis, recurrent bronchitis, the streptococcus infections in particular, should be promptly recognized and treated in these individuals. Influenza, especially, should be punctiliously treated even in its milder forms in these patients. Following any of the infections, especially after measles, scarlet fever, tonsillitis and bronchitis, an adequate period of rest should be enforced for full convalescence. The child should be immunized against diphtheria and typhoid fever. Adenoids and sinusitis should be promptly treated if they arise. Pyelitis in such families should not be permitted to drag itself along through long periods of neglect.

Measures of this character beyond any doubt materially lessen a family tendency toward cardiovascular disease of any character, and no more in any other than in the complex of angina pectoris.

The selection of a life occupation is another preventive matter of very great importance in anginal families. Certain occupations are manifestly unfitted by their normal requirements for

men of this hereditary taint. It is a very common experience in our technical schools to see young persons, study of whose history, previous sicknesses, and especially of the family history, would show that they lack ability to sustain the stresses of the elected vocation. Many young men are ruined for their life calling by negligence in this obvious matter. Such restrictions apply with particular pertinency to young men with a family tendency toward angina pectoris.

The growing habit in America of taking vacations is certainly a step in the right direction in the preventive treatment of angina pectoris, but in too many instances these tendencies are directed into wrong channels and become a detriment rather than a benefit. The physician may find, for example, on any golf course, men the subjects of real or tentative angina who under the delusion that they are benefiting their health, all untrained and unprepared from a physical standpoint, indulging in stresses well fitted for the young college athlete, but not for the mature and frequently overplump business or professional man who six days out of each week must sit at his desk, stand on the turbulent floor of the stock exchange, or under the tremendous responsibility of the operation theatre. Old men try to play tennis with their sons, to defeat them at hand ball, to outdistance them in swimming, to outclimb them in the mountains—many of them develop angina.

Once angina has developed in any patient the physician should make the most painstaking sort of study possible of that subject, of his heredity,

past history, especially as regards the infections and of his habits and obligations. The object is to detect the cause of the basic pathology, to remove it if possible, and to limit or check its ravages before permanent and unhealable lesions have developed.

The recognition of syphilis should be practically simultaneous with its vigorous treatment. It has been frequently pointed out, by Wile, Stokes, the author and others that this preliminary treatment should not be inaugurated with the arsenicals but with mercury, bismuth and the iodides. Arsphenamin in all its forms is a dangerous agent to employ in cardiovascular syphilis until the patient has been at least once brought under the full effects of the iodides, mercury or bismuth. Most cases of angina pectoris caused by syphilis can be benefited symptomatically by specific medication in conjunction with the usual general measures. Early cases may be clinically cured and even late cases greatly benefited.

Gout is a cause of angina pectoris in at least a certain number of instances. Gout can be cured in its early phases and can be more or less benefited in all except its terminal aspects. Anti-gout treatment in gouty cases of angina pectoris will usually result in benefit and occasionally cure. Atophan, colchicine, the alkalies and, above all, dietetic treatment of gout is imperatively called for in those instances of angina in which gout is a probable etiological factor.

The rôle of rheumatic infection in the development of angina pectoris has not been sufficiently emphasized in the past. Probably more than any

other one factor, rheumatic fever in any of its protean manifestations is the most frequent cause of the fibroid heart. There can no longer be any question but that fibrosis of the heart muscle is a frequent basic pathology of the symptomatic picture of angina pectoris. Early, vigorous and persistent treatment of rheumatism is beyond question at least deterrent of the development of these cardiac changes. Particularly important is the adequate recognition in these instances of necessary slow convalescence and of aggressive convalescent treatment in cases in which the heart is known to be involved. The salicylates are beyond question both protective and curative in these instances and their employment in chronic and recurrent cases is very highly beneficial not only in the prevention of angina pectoris, but occasionally also in its mitigation and relief. The value of the iodides also in those cases originating from myocardial defects is an established clinical fact. This is illustrated even in occasional cases of active angina in which the iodides and less frequently the salicylates give decided relief of the complex.

As a further illustration of the need for specific treatment in angina pectoris one may cite those cases which appear in diphtheria. I have seen but a single case however in which the administration of diphtheria anti-toxine was followed by improvement of a startling character. In this instance, as perhaps in others cited in the literature, the effect may have been rather that of a foreign proteid reaction than of a truly specific nature.

In true angina pectoris one must presuppose as a basic pathology either disease of the coronary artery, of the aorta, or of the myocardium and possible, though I believe rarely, disease of the pericardium, particularly of that portion at its application to the root of the aorta. Rest is an absolute essential in the treatment of all these lesions and so very essential is rest in the treatment of angina, both from the standpoint of relief of symptom and of improvement of causative lesion that your speaker is impelled to consider rest as one of the specific measures for the treatment of angina pectoris.

Most cases of angina pectoris benefit at least symptomatically from a period of rest in bed. In many of these cases, if not in all, rest affords a break in the habit element which plays an important part in the development of attacks and if associated with proper medical treatment it also affords a period of lessened physical and emotional stress in which reparative alterations in the essential lesion may be encompassed. Anginal attacks are, however, incited both by emotional and by physical stresses, probably no more by the one than by the other. There are instances in this disease in which confinement to bed for longer than a mere temporary period leads to such emotional stress, perhaps because of neglect of business or of other crucial obligations, that the patient is injured rather than benefited by too prolonged a period of enforced rest.

Every successful physician has seen cases of angina pectoris in which symptoms were made worse instead of

better by absolute rest treatment. Many instances have been observed by your reader in which it was found most beneficial to permit even during rest periods a certain degree of mental and physical activity. The proper determination of the degree of rest which should be utilized in the treatment of any individual case of angina then must presuppose a very intimate knowledge on the part of the physician of the character, mentality and even of the social and business requirements of the patient. Here art steps in and dominates science in the practice of medicine.

In order to be most beneficial, rest treatment must be most carefully studied and individualized. Shall or shall not the patient receive the privileges of the bathroom, must he use a bed pan, or may he use a commode? These are important matters which may only be determined by intimate knowledge of the patient, rather more than of the disease, oftentimes.

The time and manner of the resumption of relatively normal life habits after the period of rest treatment is a very important and difficult problem. Only close observation of the results in each special case can really determine this. Most cases sooner or later must resume at least an ambulatory invalidism, and in most instances it is far better and wiser that they should do so. Your reader has never seen a case of angina pectoris eradicated by rest treatment, no matter how long enforced. Angina pectoris occurs at a period of life when degenerative changes in the circulatory mechanism are naturally progressive. Too much rest, too little circulatory

demand may tend to augment the rapidity of this process. All this must rest on the judgment of the individual case. There is perhaps, no more severe test of understanding and real knowledge of medical art than is required in such cases.

In very many cases rest of a merely physical character must be augmented by the use of drugs. Those most suitable for the particular case are largely determined by the patient himself. In instances of hypertension, the bromides, chloral and similar sedatives are most useful, but where, as is so frequently the case, hypotension instead of hypertension is present, these drugs which have a hypotensive action are not well exhibited, and we turn more naturally to the opium group of drugs. They are imperative in some cases, especially those in which a coronary thrombosis has taken place. There is another drug of the sedative class which has long been recognized as of essential benefit in these cases. Of it Heberden said "Quiet, warmth and spiritous liquors help to restore patients who are nearly exhausted, and to dispel the effects of a fit which does not soon go off." It is very possible also that the euphoristic effects of the alcoholics play a beneficial role in cases of angina pectoris, but anyway your speaker is convinced that we possess in properly chosen alcoholics a very efficient weapon for the combating of angina pectoris, especially in that of the late adult and in old age.

Healthy normal sleep in abundance is the highest index of rest treatment in angina pectoris. It is essential in any phase or condition of the complex

and it must be obtained by any means possible, preferably without drugs, but if necessary with their assistance

The last few years have furnished us with a group of drugs which are of such direct action in angina pectoris, especially on the basic lesions of the complex that we may almost consider them in the nature of specifics. Your reader is not universally enthusiastic over these drugs, he has not felt that they have lived as yet fully up to the hope which the pharmacologist and particularly the foreign drug manufacturer have promised, but they are definitely valuable in many cases. They are those drugs which act, as pharmacologists affirm, through specific dilatation of the coronary vessels and possibly otherwise to improve the circulation within the heart muscle. Mostly they are modifications or adaptations of caffeine or theine. They are euphalline, theocaine and the like. Their efficiency brings to mind that before recent days coffee and tea were employed by our predecessors in the treatment of angina pectoris as in other forms of cardiac disease. Nowadays, as your reader believes, largely through the advertising activities of substituted materials they have fallen into disrepute in the management of cases of cardiac disease.

We must not neglect the subject of the nitrites and of the very large group of vasodilators in the treatment of cases of angina pectoris. Their almost indispensable character in the management of the acute attack has in some instances blinded us as to their essential value as preventives of the attack or as medical agents in the routine treatment of cases between the

attacks. These drugs through their ability to dilate and relax the arterioles may be used to excellent effect in many instances of the disease in its quiescent phases. While this is particularly true of those instances in which hypertension and arterial spasm are elementally present they often act well in the prevention of the paroxysm in cases of normal or even in hypotension. Your reader has found them particularly valuable when given at bedtime especially in those cases which develop attacks during sleep. As a rule the reader has found sodium nitrite and erythrol tetranitrate most efficient in this respect because of their slower and more prolonged effect apparently, but nitroglycerine and amyl-nitrite are also useful for this purpose. Benzyl benzoate is beneficial in this usage also, probably much more so than in any other phase of the complex.

Probably the sedatives, chloral hydrate, the bromides, luminal and the like, though chiefly mere sedatives, also act in this manner in some degree. They are all useful and which is the most beneficial in any instance can be determined only by clinical experiment in the individual case.

Certain instances of angina pectoris appear to be incited by a lack of sufficient cardiac tone, perhaps by failures in conductivity. Your speaker refers now of course to those cases which are based on a pathology of myocardial defect. In these digitalis and digitalis-like drugs act beneficially. It is the impression of your reader that in most cases of angina which originate from coronary or aortic pathology that the digitalis group of

drugs tends to make the symptomatology worse rather than better, but in those of myocardial origin, they often benefit just as sometimes we are forced to use digitalis after coronary thrombosis, contraindicated in this circumstances as it usually is. Caffeine also seems to act very beneficially in certain of these cases. It should never be pushed to the point of mental excitement. Strychnia also has its indications, as your reader believes, in those cases in which extensive myocardial lesions have resulted in a depressed muscle irritability.

Too much has probably been written on diet in angina pectoris. It is rarely of real importance. There is no diet for the condition any more than there is a specific drug treatment for all cases. We must recall again that we are not treating a disease, but an individual, with an extremely varied pathology which chanced to produce a symptomatology which happens to present a very striking and apparently characteristic picture. The individual with the complex may require a diet or may not, but there is no suitable dietary for the complex as such.

It has already been said that cases the subject of gout will require an anti-gout diet, cases the subject of grave anaemia will deserve a diet rich in iron. Obese patients as a rule will do best on a diet low in starch and fat, malnourished patients improve on a pushed general diet, and so on. Again the fact must be determined from a full consideration of the probable basic pathology and from a study of the results which follow application of these conclusions. It is a matter of clinical experiment which is quite as

scientific and infinitely more important than studies with the lower animals.

It is a commonly recognized fact that many paroxysms of angina are excited by gastric irritation or distention, by intestinal flatulence, or even by such definite irritative gastrointestinal lesions, as duodenal ulcer, chronic appendicitis, colitis and the like. Gall bladder disease is not only often closely simulated by angina pectoris, but it may also beyond doubt precipitate the paroxysm in some instances. It is obvious then that the diet problem may very rarely become of extreme importance and one may well recommend in generality that all those foods which produce difficulties of digestion, either chemical or mechanical, may be wisely eliminated.

As has been previously intimated, the writer feels that the alcoholics properly used benefit rather than otherwise. This is especially true in late adult life or in old age. The use must not be confused with the abuse of alcohol, however, and the determination as to the benefit of alcohol in any given case depends on clinical study as definitely as is the case with any other agent utilized in the disease. Wine or beer with dinner, or a highball just before retiring will not infrequently ward off attacks or much mitigate their severity.

Tobacco has been generally condemned for usage in cases of angina pectoris. The reader is one of those who believes that there is a very distinct demarcation between tobacco angina and true angina, nor does he feel that tobacco alone is ever capable of causing the lesions essential to the development of true lethal angina pec-

toris. Nevertheless he is convinced that tobacco in truly anginal cases increases the severity and occurrence of the attacks. It should be forbidden in practically all instances of the complex.

The surgical treatment of angina pectoris has received very much attention within the past few years. From a perusal of the surgical literature on the subject one is almost invariably regretful that so little conception of the essential pathology of the complex has backed surgical research and one notes almost invariably that relief of the symptoms is considered as a cure. Surgery has, nonetheless, established for itself a definite place in the treatment of angina pectoris. It is definitely and only indicated in those cases in which the severity and frequency of the paroxysm is great and in which medical management and treatment has served neither to relieve the pathology or to control the symptoms. There is still another essential qualification which the internist must consider before he turns the case over for surgical treatment. The suffering in these cases must be of a very severe, well nigh unbearable character, not relieved or rendered tolerable by medical management.

Surgery at the best but breaks the connection between the essential lesion, which is capable of causing death and which must remain as dangerous as ever after the operation as before and the symptom-producing mechanism which produces the clinical syndrome. This is all that may be accomplished by surgery, and it is quite enough to justify it in a good many intractable instances where suffering

has rendered life a mere agony and unwarranted burden. As Mackenzie prominently pointed out, the removal of the symptom or safeguard of pain and suffering probably in some degree lessens the chances of life for the patient because it eliminates the warning of the attack when the patient undertakes things which induce the complex.

Very briefly surgery in angina pectoris consists in the removal of the sympathetic ganglia or resection of the sympathetic trunks in such a manner as to block the disease impulse originating in the cardiac lesion from demonstration or appreciation through the sympathetic chain. This may be successfully accomplished in the hands of a skilled surgeon in a considerable percentage of cases. No change in prognosis is accomplished but relief from agony is well worth while in some instances.

Injection of the nerve trunks has been recommended and successfully performed by Swetlow, Schwartz and others. It acts in the same manner, though possibly in a less permanent way as the surgical procedure just mentioned. The method, although alleged to be simple, probably requires quite as high a technical skill as does any of the surgical operations. It has the same disadvantages as more overt surgery and is probably less likely to produce permanently good symptomatic result. It has a field in those instances which deserve surgery for the relief of suffering and which refuse it because of its name.

Most of the reader's time has been devoted to general treatment of angina pectoris for the reason that many



practitioners fail to realize what may be accomplished in the way of actual cure and amelioration of the complex. Little time now remains in which to consider the treatment of the paroxysm. This does not express your reader's judgment of proportions but rather the obligations of the programme. Further also the reader feels that the average practitioner is already well conversant with the matter of treatment of the immediate attacks, and there is therefore little on which your reader may instruct him.

The attack should be stopped as promptly as possible, not only because of the intense suffering which it frequently entails, but also because there can be no doubt but that attacks which are permitted to mature unquestionably tend to increase the frequency of future attacks, that is, it tends to the establishment of a habit of attacks. Even mild attacks should then receive attention, death is almost as likely to occur in mild attacks as in severe ones, but the longer the attack the more lethal it is. Hence the physician should instruct his patient to check the slight attacks and not to allow them to develop into severe ones.

Whenever the patient is seized, he should immediately stop whatever he is doing. He should assume as nearly as possible a position of rest. In many instances this alone will suffice to abort the attack. In case prompt relief is not afforded the patient should take or be given nitroglycerine in the form of the spirits of glonoin, as a tested tablet, preferably hypodermic of nitroglycerine, either swallowed with water, or given hypodermically, or given intravenously if a physician is at hand.

There is no advantage gained from retaining the tablet in the mouth until it dissolves. Some cases react perfectly to the fumes of amyl nitrite inhaled from a crushed pearl or ampoul of the drug with which he should always be provided in these cases.

If prompt relief is not afforded, the dose should be repeated, if necessary, several times. The patient should be always fully instructed as to the effects of the drug, otherwise he may be seriously frightened by its effects. A little experiment will soon demonstrate which drug and which form of it is most useful in any individual case, but it is well for the patient to be provided with both nitroglycerine and amyl nitrite in preparation for a prolonged attack without medical assistance being available.

Where the attack still persists in spite of the adequate use of the nitrites, morphine should be given, it is the drug of all others which is most universally beneficial and it may be required in very large dosage, one half grain at a dose, repeated several times if need be. Patients of strength of character who are not likely to abuse or misuse morphine, after having been fully instructed as to its indications, danger of its frequent use and the like, may be furnished with sterile hypodermic units of morphine, especially if the requirements of their life oblige their being distant from probable medical assistance in case of an attack.

The patient should not be moved until the attack has subsided. There is good reason to believe that as the attack subsides its danger also diminishes proportionately.

Self treatment is in general a very unwise thing on which to instruct a patient, especially a neurotic and emotional type, but this is a condition in which self instruction and self treatment must usually be utilized if the full and most beneficial effect is to be realized. It goes without saying that if the attack does not quickly subside or if it is soon repeated a physician should be sent for, but most intelligent patients soon learn how to

care for ordinary attacks themselves if they receive adequate instruction from their physicians at the outset.

Where attacks persist in spite of treatment or when they recur, coronary thrombosis of some extent has usually taken place, this requires persistent and careful treatment which should extend over days or even months. This is obviously a subject beyond our consideration in this crowded program.

# The Coronary Problem\*

By ARTHUR R ELLIOTT, *Chicago, Illinois*

CORONARY arterial disease presents a varied clinical picture. The abundant literature which has accumulated since Herrick's forceful and illuminating description of coronary occlusion in 1912 seems to be mainly devoted to certain of the more dramatic aspects of coronary disease, notably angina pectoris and coronary thrombosis with its consequences. This brief discussion will be concerned with coronary manifestations that are less frank and typical than the major developments referred to, in short with what has been termed because of this obscurity, "occult coronary diseases."

Outspoken sensory complaints, such as angina pectoris, may not develop from disease of the coronaries, for all grades of sclerosis and all degrees of occlusion even to obstruction of one or both main trunks have been found at necropsy in individuals who had never experienced angina. Willius and Brown in 1924 undertook an analysis of 86 autopsies, representing unselected proved cases of coronary sclerosis, for the purpose of determining the frequency of occult coronary disease. The result of this research was their conclusion that 34 of these cases

or 40 per cent might fairly be classified as occult, inasmuch as diagnosis had not been possible during life because of insufficient subjective and objective evidence. Morawitz and Hochrein recently reported one year's experience which comprised 137 autopsies where essential changes of the myocardium and coronary arteries were present. They found 91 showing extensive coronary sclerosis and of these 91 patients 75 per cent had not complained of subjective symptoms of heart disease. Without further citations from the literature we may accept the fact as proven that coronary pathology of sufficient extent and degree to bring about cardiac death may exist without attracting attention by unequivocal signs and symptoms. There is really nothing surprising about this considering the fact that vascular degeneration is the main-traveled road to old age and that some degree of atheroma of the aorta and its proximal branches is one of the almost inevitable liabilities of maturity. It is notorious that aside from the aorta, the coronary arterial circuit is more frequently the seat of disease than any other in the body. These arteries, first and most important divisions of the aorta, receive as it were at first hand the buffetings borne by the parent stem and share in large

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measure the ill effects of a lifetime's strains and stresses. Walkoff is credited by Riesman with the statement that the thickening of the intima of the coronary arteries surpasses that found in other arteries at the same age, and the statement is current (Werley) that these vessels are sclerosed twice as often as the arteries of the brain and three times as frequently as the arteries of the kidneys. Moreover, the coronaries may be found diseased while all other accessible parts of the vascular system appear unaffected. Attempts to explain this peculiar susceptibility to damage have been unsatisfactory and we will not discuss the question here further than to comment that the obvious explanation remains the most plausible, namely, their immediate geographical relationship and intimate dynamic co-partnership with the aorta.

The heart muscle because of its continuity of function must it would seem be particularly sensitive to changes in its blood supply. This appears to have received convincing proof from experimental investigation and it is well known clinically that disease of the coronary arteries is one of the most important causes of myocardial weakness. Unfortunately for the interests of clinical clarity it appears impossible to estimate with any degree of certainty either from the amount of functional disturbance or symptomatic discomfort the extent of involvement of these vessels. In one case we see death result in a paroxysm of angina or from the syndrome which we have come to recognize as coronary occlusion without there having occurred any clinical manifestations of significant

character and with a minimum of arterial pathology at necropsy. In the next case it may be there is revealed the most extensive obliterative processes without any great abridgement of the patient's activity or comfort and even large infarctions and parietal aneurysms resulting therefrom have been known to develop painlessly. Osler long ago asserted that a man might get along very comfortably although with a lowered range of efficiency upon one-fourth of his normal coronary blood supply. It seems a fair assumption that the factor of safety under such circumstances is the vascular reserve that is built up as age advances by means of new anastomatic connections within the coronary circuit and between those vessels and surrounding neighborhood arteries with some help doubtless from the Thebesian vessels. This point granted, an inference similarly drawn is that the later in life coronary obliterative developments are postponed the better tolerated they are. This indeed appears to be the case and there is testimony from many sources that the prognosis in coronary obstruction stands in a rough manner in inverse ratio to the age of the patient. An added reason for this may arise from the greater cardiac overload carried in early middle life and the greater importance of syphilis in that age group. In the sixth and seventh decades life has taken on a more leisurely pace and syphilis as a factor fades into insignificance.

The only diagnostic criteria which at present appear available for the certain recognition of coronary disease are on the clinical side, the occurrence

of angina pectoris and the development of coronary occlusion, while on the laboratory side there are certain changes in the electrocardiogram indicating more or less severe muscle damage. If we insist upon these requirements before venturing a diagnosis most of our coronary cases would escape classification. On the other hand, one may doubt whether we should espouse such liberal views as those recently advocated by Morawitz and Hochrein,<sup>1</sup> who think that we may assume with great probability the presence of coronary sclerosis clinically, if in persons of advanced age signs of heart disturbance develop, even if such are unaccompanied by pain, and that every patient of this kind is threatened with sudden death. This is equivalent to saying with a flourish of the Absolute that old age is a disease and that to the aged death is imminent. Fortunately not every old man with a skipping heart has clinically important coronary defects. Every human being who survives long enough will undoubtedly develop sclerous changes in his coronaries but these may be no more than what is going on equally in the rest of his arterial system and need not cause the heart to break pace with the body mechanism as a whole, in other words, his heart may be just as good and no better than the rest of him, and should his heart falter, so indeed may his stomach or his brain or his legs and for the same reason. In coronary disease as with defects elsewhere in the body we might perhaps draw some line of distinction between active and inactive pathology.

<sup>1</sup>Morawitz and Hochrein: *Munch Med Wchnschr*, 1928, 5 17

Not every chronically infected gall-bladder is a symptom-breeder calling for surgical removal and a man may carry a slowly enlarging prostate into a ripe age and to his grave without ever experiencing more than some frequency of urination. In similar manner the sexagenarian with a sclerotic heart but a reasonable mind may by moderating his pace live very comfortably and efficiently and never suffer an angina. This may be an illustration of what the philosopher had in mind when he surmised that "at forty every man is either a fool or a physician"—he either listens to the voice of experience and regulates his life according to its precepts or he goes the way of all fools—to destruction.

The concentration of medical attention upon coronary disease during recent years has resulted in stigmatizing various cardiac developments as coronary in origin which were not formerly suspected of belonging in that category. Notable among these are chronic myocarditis, the failing heart of hypertension and certain of the arrhythmias arising in the mature. It may prove a fair prediction that as time goes on intensive study of the coronary circulation in all forms of sclerotic cardiopathy will more and more accent the importance of obliterative changes in that circuit in bringing about functional decline. Invariable and careful exploration of these vessels as a routine in non-cardiac deaths among mature individuals and a careful coordination of such findings as are revealed with the clinical history may give us in time a more adequate understanding of the problem.

We have come to interpret angina

pectoris as a manifestation resulting from ischemia of the myocardium. Functional overload raising the nutritive demand for the moment above the level of vascular capacity elicits the tell-tale sensory protest. This interpretation helps us to a better appreciation of the symptoms of coronary sclerosis. A liberal translation of the term "angina" is essential if we are to include the various sensory discomforts, aches, pains, constrictions, pressures, burnings, etc., according to the terms of the patient's description. Bizarre in their variety they are equally peculiar in their location—in one case in the abdomen, in another in the neck or occiput, precordium, substernum, wrist or rectum. If they have any feature in common it is their dependence on overload for their production. Effort, emotion, eating, coitus are apt to infringe the sensory well being, yet the pains may arise during sleep in the small hours of the night. To the sense of alarm which is their psychic accompaniment is often added a confusion of mind, doubling the feeling of insecurity. Even when his discomforts are mild and bearable the patient's obvious anxiety hints at a tragic feeling that they represent a factor which in the end may prove his undoing. In certain cases there may exist no painful discomforts but the heart is periodically disturbed in its rhythm either by a run of premature contractions or there may occur definite attacks of paroxysmal tachycardia. The latter development arising for the first time in middle life is an extremely suspicious circumstance. Fibrillation in hypertension or with aortic atheroma is probably more frequently than not

the result of a sub-lethal coronary occlusion. In the sclerotic cardiopath any abrupt change for the worse in circulatory efficiency should be distrusted as probably the result of coronary obstruction even if no pain precede or accompany the transition. It will be agreed by experienced clinicians that a great deal of difficulty may be encountered in the satisfactory interpretation of sensory discomforts that are presumably anginal. If they are located in the upper abdomen differentiation from gall-bladder, gastric or duodenal disease may be difficult. If in the chest other structures than the heart may be to blame and the so-called radicular syndrome calls for attention. How difficult the solution of the diagnostic problem may prove is illustrated by the following case at present under observation.

On the first day of the present year there was referred to us for examination a successful business man of the high pressure type. He gave his age as 52 and related the following history. At the age of 30 he had had a severe attack of migratory febrile arthritis without visceral complications. For many years he had been an occasional intemperate user of alcohol and was always a heavy smoker of cigarettes. When 49 years of age he passed a kidney stone, was cystoscoped and infected and his urine has ever since contained pus. One year before consultation toward the end of a period of unusual business strain he suddenly experienced a burning pain in his epigastrium with rapid fluttering action of the heart and dyspnoea. He presently broke into a profuse perspiration and with that the attack passed off

leaving him strangely exhausted Two months later this experience was repeated rather more severely. On this occasion as before, the sensory discomfort was epigastric in location with limited radiation upward along the left border of the sternum but not into precordium, shoulder or arm. The heart fluttered and he had a desire to belch He was dyspneic and sweat profusely These discomforts persisted but a few minutes and left him feeling weak, anxious and depressed Following this second attack there occurred at irregular intervals especially if he ate or drank heavily or became excited, milder discomforts somewhat similar except in degree to those described About the middle of November he has his most severe attack This wakened him from sleep and lasted three-quarters of an hour He sat rigid on the side of his bed afraid to move and bathed in a cold clammy sweat Morphine was administered by his physician Although he had recovered satisfactorily from previous attacks, this last one left him weak and dyspneic and he had not regained his former comfort or efficiency at the date of our consultation six weeks later Hardly a day passed in the interim that he did not experience some sensory discomfort These were not always the same and analysis of his symptoms as described enabled one to separate pretty definitely three different kinds of disturbance At irregular intervals he would have attacks of fluttering heart action, dyspnea and clammy perspiration with exhaustion afterward At other times and much more frequently there would occur a sense of epigastric burning radiating

upward with a desire to belch and if he succeeded in doing so relief was instant A third complaint was of frequent vague feelings of aching and soreness in the precordium and lower left costal region These often occurred at night and were to some extent but not always amenable to changes in position. The essential findings brought out by physical examination were an easily appreciable degree of general arterial fibrosis, a slightly enlarged heart with distant unsatisfactory tones, the pulse rapid but regular, blood pressure 130/100. There was no evidence of circulatory stasis The prostate was smoothly symmetrical but slightly enlarged and the urine sediment contained much pus and a few casts Here then we have a clinical history pointing clearly enough to the heart and the nature of his symptoms made it likely that he had coronary sclerosis The varied character of his discomforts and the meagreness of the physical findings rendered the problem a very interesting one to unravel He remained ten weeks under close observation and the upshot of the investigations may be summarized as follows

The electrocardiograms showed low amplitude in all leads with isoelectric T wave in lead I The amplitude improved under rest and digitalis but did not reach normal. X-ray measurements of the heart gave a cardiothoracic index of 44 per cent, the great vessels measuring 7.2 cm. with undue prominence of the aortic arch There were revealed definite arthritic changes involving the anterior and posterior surfaces of the dorsal vertebrae especially clear about the fifth and sixth

Gastro-intestinal barium fluoroscopy revealed nothing of importance except that there was found to be a gastric diaphragmatic hernia which measured about one and one-half inches in diameter through the esophageal hiatus of the diaphragm. Basal metabolism and blood chemistry were within normal limits and the Wasserman test was negative.

While under observation in the hospital there occurred three attacks of substernal oppression with fluttering of the heart identical in every feature with the three attacks included in the clinical history. These sensory discomforts were found to represent paroxysmal tachycardia, the rate in each instance going to 180-200. Their duration was from ten to fifteen minutes and they were accompanied by a profuse clammy sweat. Two of these paroxysms were promptly controlled and terminated by pressure on the vagus in the neck.

When this patient's sensory symptom complexes are checked against the above findings we perceive that there is a reasonable explanation for at least two of them. His attacks of epigastric burning sensation after meals relieved when he succeeds in belching may be accounted for by the presence of a small gastric herniation through the esophageal opening in the diaphragm. Release of air tension in the gas bulb of the stomach by belching brought him instant relief. We have in this mechanism a satisfactory explanation of one subdivision of his sensory disturbances which removes it outside the range of coronary effects. In similar manner, a second symptom group may be disposed of by attributing to the osteo-arthritis in the mid-

dorsal spine the causation, through nerve root irritation, of the persistent soreness and pain in the precordium which was according to the patient's experience more or less constantly relieved by changes in posture.

There remains as a concentrate after thus deleting two of his three suspicious symptom groups, the paroxysmal tachycardia to be accounted for. This did not develop until the patient was fifty-one years of age, after years of excesses and hard nerve-wracking work. This fact raises at once the presumption of myocardial damage as an etiological background. Other cardiac phenomena present consisted of a persistent low pulse pressure, a decidedly equivocal electrocardiogram, rapid rate, poor heart tones and generalized arteriosclerosis. Time alone will tell how severe the encroachment is on this patient's coronary blood flow, but I feel sure it will support the conclusion that there exists serious obliterative coronary endarteritis.

Experienced internists will see in the foregoing briefly related case incomplete and unconcluded as it is, an illustration of the difficulties that this problem is constantly presenting for solution. Many times certainty of decision as to whether important coronary defects are the direct cause of complaints is for the moment impossible, the matter being left for Time to decide. Where clinical grounds are insufficient special methods of investigation, such as x-ray and electrocardiography, may decide the point. The high incidence of certain graphic abnormalities in proved cases of coronary disease makes the electrocardiogram a valuable adjunct in interpreting the clinical problem. Variations may be



revealed in the tracing that center attention at once on the coronaries and may thereby aid decisively in the identification of the occult type of coronary sclerosis. Careful clinical study

with meticulous care to secure a complete and detailed history aided by routine electrocardiography furnishes the best guarantee of solving this difficult diagnostic problem.

# Fatigue and Infection

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THE title of my paper, "Fatigue and Infection", will bring many different concepts to the minds of those reading it. What do you and I mean by the word "Fatigue", and what do we mean by the word "Infection?"

In a general way, we believe Sir James Paget's dictum to be true when he says, "You will find that fatigue has a larger share in the promotion or transmission of disease than any other causal condition you can name"

There are so many kinds of fatigue that our ideas are apt to be too general or too limited. Muscular fatigue comes to most of us as the best example of fatigue but we usually, even here, fail to appreciate that it is not a local or circumscribed phenomenon but a complicated condition of failure in the efficiency of the whole organization to meet the particular demand<sup>1</sup>. We further recognize that training delays the onset of fatigue but it is not easy to say just what this training accomplishes, or the mechanism of its production. The fundamental conception is concerned with the reactions of certain cells or groups of cells to certain kinds of stimuli. Among the innumerable stimuli to which the cells of our body respond are those arising

from the presence of microbes. Such stimuli often demand reactions in cells with other specialized functions, and the failure to adequately respond may be due to many factors such as previous over-activity or under-activity, interference with blood supply, faulty diet and similar general nutritional deficiencies.

However difficult it may be to define the normal condition of cells, at least we think it normal that cells should resist the displacement by other cells, particularly such foreign cells as those of bacteria. Normally the cells of the body are resistant to bacterial infection and the failure in this resistance is, in many cases, simply a failure to react,—a fatigue in the normal mechanism of defense. In the beginning, the defense is simply the healthy metabolism of the cell, the bacteria not coming in contact with the cell, or, if they do, the conditions normally do not favour the invaders. The fatigue of any cell makes it a more easy prey to the microbes. The mere massive onslaught of large doses of bacteria, as so often used in experiments may undoubtedly break down our defenses but such, in the natural history of infection only occurs under the rarest conditions. Bacterial invasion is very common but a recognized infection seldom follows. Infection

<sup>1</sup>Read before the Boston meeting of the American College of Physicians, April 9, 1929

depends upon the ability of the parasites to multiply in the host; this ability we call virulence, and it is developed and maintained in the host. We recognize disease only in those cases where the outcome has favoured the microbe, but we know little in most of our infections about these favouring conditions

We have in the past undoubtedly over-emphasized the dominant position of the microorganism as the exclusive causative agent in the infectious diseases. The numerous factors which determine the invasion, the establishment of the microbe, the beginning development of virulence, the production thus of strains of bacteria capable of epidemic spread or of becoming a menace to the host,—these factors must be correlated and studied more critically

The portals of entry in most of our infectious diseases are through the mucous membranes. The important defense against the first stoppage and primary colonization, when the bacteria have entered the oral cavity, is the simple mechanical removal by the flow of saliva and the mucous secretions in the rather definite courses so well demonstrated by Bloomfield.<sup>2</sup> Sufficient secretion for this purpose is therefore the first essential in this relatively simple defense. The conditions producing fatigue of this mechanism are more or less recognized but certainly not fully appreciated. The long continued breathing of dusty air tires the secreting cells and the mouth and throat become dry. A hot dry atmosphere may similarly cause fatigue by the excess activity in keeping the inhaled air moist, while a hot moist at-

mosphere causes almost as disastrous a result by the congestion and hyposecretion of a thicker, more tenacious mucus.

These cells are further brought under stress by reflexes from the skin in chilling, and an ischemia of the mucous membrane results. Among other factors, faulty diets of various kinds play a leading part. The striking replacement changes in the cells of the mucous membrane of certain parts of the respiratory tract from vitamin A deficient diets as shown by Wolbach<sup>3</sup>, indicate that the whole functional activity of these cells may be lost. Hoelzel<sup>4</sup> has shown the importance in the production of colds, of edema or hydration of the organism, which develops under a restricted protein and a high carbohydrate diet. Chilling of the highly hydrated and sensitive skin throws an overload of fluid on the already overloaded respiratory tract and an excessive secretion follows. Cheney<sup>5</sup> has stressed a disturbance of the acid-base equilibrium with conditions favouring a mild acidosis, and advocated alkaline treatment. Many investigators have emphasized the beneficial tonic effects of regulated exercise and the harmful results of general fatigue, constipation and similar strains. The influence of all such factors must be carefully considered in arriving at a composite picture of the mechanism favouring infection. In its simplest form it may be said that a mucous membrane with a good reactive tone prevents bacterial localization and hence infection, while a tired mucous membrane failing to react, invites it. These infections may be the beginning of the most serious acute diseases such as pneumonia, or

the bacteria involved may lead to localized infections and the establishment of infected foci which serve the bacteria as outposts from which further invasion and infection may follow later, and such outposts often act as a long-drawn irritation to the body and may alter the whole type of cellular activity so that we develop the type of allergic reaction which Swift<sup>6</sup> and others have been studying in rheumatic conditions. Allergy in the cell is in many ways analogous to the familiar fatigue phenomenon in which an individual at a certain stage of tiredness is hyperactive, highly irritable and often does more harm than good to himself and his associates. Certainly in the rheumatic type of reaction the acute onset is frequently ushered in by a variety of events in which fatigue is a marked feature, and today more attention is being given to the factors bringing on this state in which a minimal stimulus brings about a maximal result. Fatigue of inhibitory mechanisms is a form of fatigue demanding more attention.

Under the circumstances of life, there is a far better hope that we may learn how to prevent the fatigue conditions of the respiratory tract than that we will ever be able to effectively interfere with the spread of oral bacteria from mouth to mouth.

The other common portal of entry for bacteria is the intestinal tract and it has other interesting and important bearings on the subject of fatigue and infection. Heavy exercise and fatigue definitely interfere with gastric secretion largely due to the disturbance of circulation. Another recognized factor is the external temperature and for

much the same reason. The effect of this lessened secretion results in an increase and change in the bacterial flora of the upper part of the small bowel due primarily to decrease in the disinfecting action of the hydrochloric acid. This is of particular importance in young infants during hot weather but is certainly not confined to them. We know comparatively little about the conditions favouring the primary infection in even such a well studied disease as typhoid fever, but there is evidence to suggest that here again the healthy mucous membrane is remarkably resistant. Intestinal irritation with diarrhea or constipation plays a part in the invasion, and much experimental evidence indicates the importance of diet and the external temperature. Sir Leonard Rogers<sup>7</sup> has correlated the rise in the absolute humidity (which occurs in warm, muggy weather) with the rise in the incidence of cholera in India and might not this be partially explained by the reflex fatigue effect on the intestinal mucosa from the congestion in the skin? The seasonal variations in the occurrence of intestinal diseases have not been adequately explained.

Constipation is of many kinds but in its consideration we must not neglect the importance of fatigue. The general effect of constipation is at first a stimulation as manifested by flushed skin and a feeling of general well-being. This is followed by a stage of capillary fatigue with cutaneous pallor, headache and general depression,—all evidence of faulty circulation. These are the symptoms of autointoxication and a bowel movement relieves them so promptly that it suggests such a

reflex mechanism as the cause. Such disturbances in circulation are felt in all parts of the body and have an important effect on bacterial infection. It is common practice in the treatment of many kinds of infection to take precautions against constipation and the remarkably rapid cures after the use of laxatives are otherwise difficult to explain. Vitamin B deficient diet brings about intestinal stasis, and a deficiency in vitamin A a tendency to diarrhea, and it is the fundamental cellular changes which result from these deficiencies which must be included in the many factors bearing on the fatigue of the defense mechanism against bacterial infection of not only the mucous membrane but all the other tissues of the body. Flinn,<sup>8</sup> in a study to determine the action of acid sodium phosphate in delaying fatigue concluded that the good results were due to the beneficent stimulation of the intestinal tract.

Boycott and Price-Jones<sup>9</sup> have demonstrated a marked increase in the susceptibility of fatigued rats to fatal infection after feeding the Gaertner bacillus, although no such effect was noted after subcutaneous or intraperitoneal injections.

Invasion from the intestinal tract occurs much more frequently than is generally realized but under normal conditions the bacteria are stopped and destroyed in the liver, glands and other organs.

There must be more than mere passage of bacteria, into or through these outer defenses, before an infection will follow. It takes time for the invading organisms to establish themselves in some favourable location

where they are able to multiply, adapt themselves to the new environment and overcome the immediate defense if they are to bring about an infection. The numerous failures on the part of the invaders pass unnoticed and we fail to appreciate how effective the normal defense really is.

There are so many types of infection that it would be impossible to consider them all at this time. The idea I would here emphasize is that under the stress of infection, fatigue much more readily ensues. The rationale of all treatment is to prevent this overwork so that the cells may return to their normal metabolism and regain their resistant tone. The difficulty is to determine what may be the factors inducing fatigue. Sometimes too much, sometimes too little of a special constituent of the diet, general muscular overwork and, perhaps more frequently, underwork, excess in cutaneous reflexes of various kinds, worry and a thousand and one things lead to the lowering of reserve energy and thereby prevent the recovery.

There are, however, certain localizations in which the difficulty in obtaining mechanical rest plays the dominant rôle in keeping up chronic and even acute infections. The infected foci about teeth and tonsils, the infected ulcers in the stomach and duodenum, and in the colon are examples of those difficult to keep at rest.

In the tonsils, primarily infected under the circumstances of invasion already discussed, incident follows incident until there is a chronic infection deep in the thin-walled crypts of the tonsil where there develop ulcers surrounded by numerous blood capillaries.

In the act of swallowing, the tonsils are definitely massaged which undoubtedly forces bacteria into the circulation, the numbers increasing under acute exacerbations because of actual increase in the bacterial population and the increased blood flow associated with the inflammation. Patients with tonsils of this kind become conscious of the infection under a variety of fatigue conditions, the margin of safety being much reduced. The tonsillar infection also plays a part in inducing the fatigue and it is the vicious circle thus established that makes so difficult the interpretation of the primary causes of the fatigue syndrome. Although many preventive measures may help to protect against the original fatigue conditions which permitted the primary infection, once this becomes established, it is the most important complication and the tonsils should be removed, principally because of the potentiality of the bacteria for infinite multiplication at the expense of the host. It is too much to expect, however, that the elimination of such foci will in all cases simultaneously remove the original causes of the fatigue state, but very often it does give invaluable aid in re-establishing a better cellular tone and resistance.

We have similar conditions to consider about the teeth. Corresponding to the thin epithelial lining of the tonsillar crypts we have in the gingival crevice the weakest link in the chain of epithelial covering in the mouth. There is further a very rich capillary blood supply which in cases of pyorrhea is increased. Pyorrhea develops in the great majority of cases because of unusual strain on the

gingival tissue. The commonest cause of this strain is malocclusion with its continuous excess pressure on one side and drag on the other. There is, of course, normally a good deal of movement of the teeth which is a healthy stimulus to the surrounding tissues but when this becomes excessive, fatigue ensues and all manner of mouth bacteria and even amebae move into this area of lowered resistance. The effective cure of pyorrhea is to adjust these stresses, this gives relative rest to the tissues and there usually follows a remarkably rapid return of the normal tone and with this an automatic elimination of the infection.

When periapical infection has resulted from the many familiar causes, it is the continual movement of the teeth which prevents cure. This movement is not only in mastication but practically every time we swallow. The problem of discovering this type of infection is beset with difficulties. Dental films, although most valuable, are of limited use and may lead us astray. There is, however, a clinical observation which has not been sufficiently stressed but which may be helpful in this maze of confusion. It is the frequent evidence of tenderness about areas of active infection which is only noticed when the individual is tired out physically or mentally. Taking advantage of such general fatigue in discovering the sites of infection where, because of the infection, the normal reserves are at a minimum and unusual reactions occur, is, I believe, a method not widely enough used or appreciated. Certainly every clinician knows and uses such methods in a general way. Our weak spots become evi-

dent under stress but it is perhaps not sufficiently recognized that the activities of infected foci rise and fall in inverse ratio with the rise and fall of the bodily reserves

The factors favouring the production of gastro-duodenal ulcers are not unlike in principle those we have mentioned for other areas. The disturbing effects of mental strain and worry, the use of locally irritating and hyperstimulating foods and the numerous reflexes affecting the circulation and hence the activity of the secretions and the metabolism of the cells, all may lead, alone or in combination, to the point of cellular fatigue where infection again complicates the process. The frequently satisfactory results of simple means of giving rest certainly speaks against the primary dominant importance of bacteria in the etiology, but should not blind us to their extremely dangerous rôle in complicating the condition and where their source is in other infected foci these should certainly be attended to

Chronic ulcerative colitis is often the aftermath of amebic or bacterial dysentery. In the idiopathic types the etiological factors are far from being clear. We are still under the spell of the early days of bacteriology. We want to discover a specific etiological cause. In my opinion we would better focus our attention on obtaining more precise ideas of the physiology of the colon, the effects of diet not only on the intestinal contents but on the nutrition and healthy metabolism of the bowel wall, the whole question of nervous impulses to and from the colon, the reasons for the extremely high incidence of constipation more

or less chronic or alternating with conditions of diarrhea. I have endeavoured to keep before me these principles of fatigue and infection in an attempt to correlate what we know about the health and diseases of the colon. Ulcerative colitis is to me a stage in a long process in which the previous stages have often gone undiagnosed, which is also true for most of the other conditions of infected foci I have discussed. The bacterial infection is very important locally but these ulcers may further serve as portals of entry for bacteria to the rest of the body. The complicating bacteria are, however, in my opinion, those of the individual patient

In the infections of other organs and the localizations of bacteria which have invaded the blood stream, we should consider as a most important factor the probability of overwork and fatigue not only of the whole body as in muscular exercise, but in the hyperactivity of any organ or tissue lowering its reactive resistance to the establishment of infection. A number of experiments such as those by Spaeth<sup>10</sup> tested the resistance of animals after forced running by means of intraperitoneal injections and found it raised. The greatest fatigue, however, in such cases is apparently in the mucous membranes and not in the serous cavities

Exercise of all the functions of the body is the surest way to prevent infection by building up a reserve of reactive energy to meet emergencies. The trained athlete from long experience and empirical practice has learned that after active exercise it is dangerous to slow the circulation too rapidly

so he wraps himself in warm blankets, is massaged and has a "rub-down" The ordinary individual feels superior to such treatment and in such cases unaccustomed exercise often results in more harm than good During exercise, bacteria may readily enter the blood stream through the dilated capillaries about infected foci when such exist but the chance of these bacteria being stopped in those organs responding to the stimuli is probably at a minimum After exercise the sudden closing of capillaries and the slowing of the circulation not only favours localization of bacteria but because of the failure to remove the excess metabolic products, offers in the fatigued tissues, areas of lowered resistance to infection. All such conditions of fatigue do little more than temporary harm unless complicated by infection and the very real menace from infected foci depends on this fact

The far more common type of fatigue is from long continued stimuli of many kinds which result, not in healthy reaction but rather in the fatigued state of sluggish and delayed reaction The fatigue associated with infection is far more frequently the result of under than of over-exertion The outstanding significance of fatigue in diseases like tuberculosis need only be mentioned but it should be realized that our success in the treatment and prevention of this disease has been almost exclusively due to the recognition of the factor of fatigue<sup>11</sup>

The therapeutic use of rest is the basis of practically all our methods of treating established infection Every effort is made to reduce to a minimum any accessory calls on the infected tissue so that its entire metabolism may be devoted to its recovery How effectively we obtain this rest largely depends on how thoroughly we understand the metabolism of the cells and how well we are able to bring about, in addition to the general rest, the physical local rest of the part

As a student at McGill many years ago, I was much impressed with that surgical classic, Hilton's "Rest and Pain" The principle he outlined still holds good,—the obtaining of physical and physiological rest by every means in our power where Pain is the monitor and Rest the cure Today we may somewhat extend the principle and say with Fatigue the warning, Pain the monitor, Infection the punishment and Rest the cure Fatigue and Infection—our efforts should be directed to know more and more about the earliest onset of each for they bear a close relationship to each other and the subject is in my opinion at the very foundations of preventive and curative medicine

After all, a paragraph in one of our daily papers under the heading "Isn't it the Truth?" gives pretty nearly the gist of what I have been saying It says, "The reason there were so few fatalities in the recent epidemic of influenza was because he-men were not ashamed to stay in bed"

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# Tobacco Smoking and Gastric Symptoms\*

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THE increasing incidence of tobacco smoking and the increasing frequency of functional gastric disorders prompted the following study, in order to correlate the occurrence of gastric symptoms and tobacco smoking, as well as to determine, if possible, the effect of tobacco smoking in individuals with organic gastric disease. Observations have been recorded during the past five years on all patients who presented themselves with gastric symptoms and who gave an associated history of tobacco smoking. For purposes of study, 400 individuals were chosen and divided into two groups. In Group A were placed 300 patients who had functional gastric disturbances and who gave a history of tobacco smoking. In Group B were placed 100 patients with organic gastric disease who gave an associated history of tobacco smoking. The ages of the patients in both groups ranged from 25 to 65 years, and there was a history of tobacco smoking for at least 5 years. Of the entire group under observation 5 per cent were women. They all presented gastric disturbances which were functional in nature.

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The chief poison in tobacco is nicotine. Other products which are formed in the process of combustion are chiefly pyridin, ammonia, and carbon monoxid. These products have a secondary and very slight effect on the system. That nicotine is the principal agent of tobacco that causes gastrointestinal disturbances has been pointed out by Cramer, Lickint, Noah, Rolleston, and others. Nicotine is one of those alkaloids that has a peculiar affinity for the autonomic nervous system, first stimulating and then depressing the sympathetic and parasympathetic ganglia. The explanation for the fact that nicotine exerts a greater action on the sympathetic is, in the opinion of Cannon, Aub, and Binger, due to an increased output of adrenalin. After nicotine injections in animals they examined the blood of the vena cava and were able to prove that there was an increase in adrenalin output.

Skaller, in animal experimentation, came to the conclusion that nicotine acted through the blood-stream on the ganglion cells in the gastric wall, and not in the sense of increased secretion of the secretory glands, for after injections of atropin the nicotine lost its action. This author also showed that it was not the nicotine saliva that caused the gastric flow, because after subcutaneous injections of nicotine sub-

stances there followed an increase of gastric juice

When we come to the question of symptoms in human beings which may be associated with the use of tobacco, we cannot altogether apply experimental observations on animals after use of pure nicotine to clinical results on humans. It should be remembered that the action of nicotine is continuous during the entire day in human beings, and that the symptomatology is not only the result of a local action on the tongue, the mouth, and the gastric mucosa, but mainly the result of stimulation of the vegetative nervous system. We find in the stomach ganglion cells whose chief function it is to promote all automatic movements after complete severance of all extrinsic nerves. We know also that both motor and secretory fibers are contained in both components of the vegetative nervous system.

The question as to the exact manner in which tobacco smoking may produce gastric symptoms cannot be definitely answered, for even after animal experimentation there are conflicting opinions. Results that are obtained in animals surely cannot be applied to the human, who readily establishes a tolerance to nicotine and smokes a nicotine containing product and absorbs, or swallows, varying amounts.

The individual sensitivity to nicotine and the art and manner of smoking have a great deal to do with gastric symptomatology. Bogner has shown that the inhaler absorbs eight times more nicotine than the mouth smoker.

Dixon states that nicotine is one of the most fatal and lethal poisons known, and the amount present in one

cigar, if injected intravenously, would represent two fatal doses to man. This author also states that the effects induced by smoking are entirely due to this principle. During smoking a part of the nicotine is burned off and a part is inhaled with the smoke as free nicotine. The drier the tobacco the greater is the destruction of nicotine. Moist tobacco evolves more nicotine and produces more serious effects than dry tobacco. It has been stated that the moistness of tobacco is chiefly responsible for many of the evils of smoking. The moist content of the tobacco must, therefore, be considered as more harmful to the smoker than the actual amount of nicotine. During the slow combustion of a cigar in ordinary smoking there is an area immediately behind the point of combustion in which the active principles of the smoke condense. During aspiration the solid gases are drawn through the moist and cooler area, carrying with them the volatile principles, of which nicotine is the most important. The cooler the smoke and the more complete the combustion, the less likely is the smoke to contain volatile toxic bodies. A cigarette or a slender cigar, as it is cooler than a thick cigar, will yield fewer of the toxic products. Many smokers realize that a fat cigar is more powerful in its effects than a long slender cigar of similar tobacco. This also explains the unpleasant effects of relighting a half finished cigar. In smoking, the degree of moisture, the tightness of the packing, the thickness of the cigar or cigarette are the most important factors in determining the amount of nicotine which will be present in the smoke. Lehman has

shown that from 1 gram of cigar there is retained, or absorbed, from 0.3 to 0.8 gram of nicotine, and from 1 gram of cigarette from 0.4 to 0.5 gram will be retained. It must not, however, be assumed that all the nicotine in the smoke is necessarily absorbed into the system.

In the analysis of the 300 patients comprising Group A, or those with functional gastric symptoms and tobacco smoking we made the following subdivisions.

1. Heartburn . . . . .	180
2. Duodenal ulcer symptom-complex . . . . .	51
3. Gastrocardial symptom-complex . . . . .	16
4. Gastrosplasm (including cardiosplasm and pylorospasm) . . . . .	30
5. Gastritis? (anorexia, malnutrition, etc) . . . . .	23

In the study of these 300 patients thorough examination was made in order to exclude organic disease in either the stomach or other organs that might account for the symptomatology. After careful history taking and physical examination, complete laboratory investigation, including chemical, serological, and roentgen studies, were done so that we were confident the symptoms present were functional in nature.

1. Those patients who presented themselves with heartburn as their principal symptom formed the majority in this entire group. Heartburn is not a disease, but a symptom due to regurgitation of gastric contents into the esophagus. As pointed out by Hurst, the mucosa of the esophagus is distinctly sensitive to chemical stimuli, and it is the presence of gastric

contents in the esophagus that is responsible for the symptom designated as heartburn. In many of these individuals heartburn was associated with a burning sensation, either in the epigastrium or in the throat. It was not dependent upon gastric hyperacidity, as has been frequently shown. In this series, of 180 patients, 97 had normal gastric acidity, 44 had hyperacidity, 37 had subacidity, while 2 had anacidity.

The frequency of heartburn in many patients with gastric symptoms, due either to local or to remote causes, has never been satisfactorily explained. Perhaps the increased salivation that accompanies smoking is frequently swallowed and the saliva in its passage through the cardio-esophageal junction at frequent intervals during the day may allow of regurgitation of gastric contents into the esophagus, thus producing heartburn. The intensity and duration of this symptom varied greatly, but was especially evident when the individual smoked between meals or on a "fasting" stomach. Some of these patients had to take bicarbonate of soda for relief of their symptoms. The amount of smoking was no criterion for the occurrence of heartburn. Approximately one-fourth of the entire number had this distressing symptom, although they smoked comparatively little. Cessation of smoking would bring about relief within 24 to 48 hours, but heartburn would recur if the patient resumed smoking. In some of those who smoked quite heavily the removal of tobacco would in the beginning be associated with loss of appetite and with gastric disturbances. It was difficult to decide whether these symptoms were

dependent upon organic changes or upon suggestion.

2 There were 51 patients, or approximately one-sixth of the entire group, who gave, upon history taking, the symptom-complex commonly met with in duodenal ulcer. Pain one to three hours after meals with epigastric distress, relieved by alkalies, was the usual story. Several of these patients had mild attacks of pain during the night, which was relieved by the taking of bicarbonate of soda. Repeated fluoroscopy and x-ray study failed to reveal any evidence of duodenal ulcer.

That symptoms of duodenal ulcer can be produced by the excessive use of tobacco was called attention to by Wagner. In heavy cigarette smokers Adler also obtained a history that closely resembles that of peptic ulcer. In this group 40 of the 51 patients were between the ages of 40 and 52 who gave a history of the use of tobacco for a period of more than 15 years. The question of tobacco smoking as a factor in the production of peptic ulcer and gastric neurosis was investigated by Barnett, who states "There is no proof that smoking is of any importance in the etiology of peptic ulcer or gastric neurosis, and secondly, there is no proof that smoking has any effect upon the age of incidence of gastric or duodenal ulcer." These individuals who present the symptom-complex of duodenal ulcer at times tax the ingenuity of the examiner, and the question of a probable mucosal ulcer in the first portion of the duodenum, despite the negative x-ray, might be entertained were it not for the fact that with the cessation of smoking the symptoms would grad-

ually but definitely disappear. If after the disappearance of symptoms these patients were allowed to smoke, there would be a return of their subjective symptoms within one week. Fractional gastric analysis showed a hypersecretion in practically the entire group. Hyperacidity was present in 20 per cent of these patients, the remainder having normal acid figures. In none of these individuals was there a sub-acidity.

3 There were 16 patients who presented the symptom-complex described by Roemheld as the "gastro-cardial symptom-complex." They were all between the ages of 50 and 65, and gave very little variation in their history. Occasional feeling of anxiety, tachycardia, oppression in the region of the lower chest, or in the upper epigastrium, breathlessness, slight distress after eating—coming on shortly after food—and the ages of the patients gave one the impression that the underlying lesion was probably arterial or cardiac in origin, rather than gastric. Some of these upper abdominal symptoms may have been due, as Rolleston states, to attacks of angina abdominis, precipitated by spasm, induced by smoking, similar to angina pectoris arising from coronary artery spasm. Because of the age of the patients and the predominating cardiac symptoms, studies of gastric chemistry were not made in this group. Moderation in the use of tobacco brought about improvement in their symptoms. Three of the patients who ceased smoking entirely had complete relief of their distress.

4 Gastrosplasm, including cardiosplasm and pylorosplasm, occurred in 30 patients. Of this number 6 had

a distinct cardiospasm of varying intensity only upon tobacco smoking. Two of these patients were physicians who had become so sensitive to tobacco smoking that the use of one or two cigarettes would produce a feeling of distress behind the sternum and upper epigastrium. All these individuals were of the nervous type, very active in their work, rushed through their meals, and were heavy smokers. Fluoroscopic examination of this group with cardiospasm showed a slight delay in the passage of the barium meal through the cardioesophageal orifice with increased retroperistalsis. Cessation of smoking brought about relief of symptoms, but a complete return to normal did not follow until about two months after smoking had been entirely discontinued.

Pylorospasm occurred in 22 of this group. There were others in the entire group (Group A) who presented occasional clinical symptoms and had x-ray evidence of mild gastrosplasm who were not included in this study. These patients under discussion had definite signs and symptoms of pylorospasm which had persisted to a varying degree for months. Their symptoms would usually come on from two to four hours after meals, and the distress would always be aggravated upon smoking. According to Carlson and Lewis, the hunger contractions of the empty stomach on smoking depend upon the strength of the tobacco. It is interesting to note that in three of these patients with pylorospasm tobacco smoking, when the individual was "relaxed," would bring about relief of symptoms. The ages of the patients in this group varied from 26

to 40 years. One-third showed a distinct gastric hyperacidity, and two-thirds showed normal acid values. There were no patients with subacidity or achylia.

Upon fluoroscopy there was increased tone and peristalsis in all these patients. The spasm of the pylorus varied in intensity and duration, but there was no paradoxical residue, and the emptying time was normal.

One of our patients, H. R., a young man of 28, had symptoms of pylorospasm of varying degree, and because of an attack of hematemesis was admitted to the hospital. Prior to his admission, repeated fluoroscopy and x-ray study failed to show any evidence of ulcer, but there was always a marked spasm of the pylorus. Because of his subjective symptoms, which terminated in an attack of hematemesis, operation was performed. A most careful examination of the stomach and duodenum failed to reveal any evidence of ulcer. This young man was in the habit of smoking from 30 to 40 cigarettes a day for five years prior to his operation. After his recovery, cessation of smoking brought about a gradual improvement in symptoms and he has remained perfectly well since.

5 In the final classification of those who presented functional gastric disorders and gave a history of tobacco smoking were grouped 23 patients who complained of anorexia, abdominal distress of varying nature, gastric disturbances, and who were underweight. In several instances, because of the emaciation, carcinoma of the stomach was suspected. The ages of these individuals ranged from 45 to 63. Frac-

tional gastric study showed normal acidity in 3, subacidity in 14, and anacidity in 6. Because of their symptoms, general appearance, and chemical findings, the diagnosis of a probable gastritis was made.

Fluoroscopic examination showed a decrease in tone and peristaltic activity, and an increased emptying time because of a somewhat patent pylorus. In none of these patients was there a history of diarrhea as occurs in some individuals with a gastric anacidity. In a special study of 6 patients who had a subacidity and in whom tobacco had been withdrawn for a period of three months there was no increase in appetite, and very little increase in weight.

The pathologic-anatomic findings in the stomachs of tobacco users are not very well known. Local changes, such as ecchymosis, inflammation, and punctuate areas of erosion in the gastric mucosa of animals that had died of nicotine poisoning, have been reported by Taylor. A chronic catarrhal process of the mucosa was reported by Grossman and Giano as occurring in dogs that had been fed for a period of several months on a watery solution containing nicotine.

Group B was comprised of 100 patients with organic gastric disease who gave an associated history of tobacco smoking. In this group were

- |   |    |
|---|----|
| 1 Duodenal ulcer  | 63 |
| 2 Gastric ulcer   | 12 |
| 3 Carcinoma of the stomach  | 6  |
| 4 History of ruptured duodenal ulcer successfully operated on by closure of the perforation | 2  |
| 5 History of posterior gastroenterostomy for duodenal ulcer                                 | 17 |

All these patients had been under care for at least nine months, and the relationship between tobacco smoking, clinical symptoms, and gastric secretory findings had been noted. The diagnosis in each case had been established by the x-ray examination, or by surgery.

1 In the duodenal ulcer group tobacco smoking was found to cause an increase in secretion in 50 of the 63 patients. If the patient smoked before breakfast, there was found almost constantly an increase of secretion of 10 to 20 cc in the fasting stomach content. Smoking caused an increase in acidity in about one-fourth of the entire group. Two patients showed distinctly lower acid figures after tobacco smoking. In the remainder the gastric acid curve was unchanged.

In 35 of these patients active clinical symptoms were present. The amount of tobacco used varied greatly. It was difficult to decide, because of the individual sensitivity, in what manner to curtail the consumption, and it was, therefore, deemed advisable to exclude the use of tobacco entirely in order to see what effect complete abstinence would have. The patients' co-operation was invited and the purpose of the test carefully explained.

We who are tobacco users know how difficult such restrictions are. All these 35 patients promised faithfully to adhere to the test for one month. All had been under ambulatory treatment prior to the test and were told to continue as heretofore, except that smoking was to be entirely discontinued. With the cessation of smoking there followed improvement in symptoms in 6 patients within one week. At the

end of a month 11, or approximately one-third of the entire number, reported distinct improvement. In the remainder subjective symptoms of a varying nature persisted. In 3 of the 11 patients who showed a distinct improvement there was loss of night pain, which had been one of their troublesome symptoms. When these individuals resumed tobacco smoking, clinical symptoms reappeared in about three to six weeks.

2 In the 12 patients with gastric ulcer tobacco smoking caused a hyperacidity in 5. Three patients showed a subacidity after tobacco smoking. Four were unaffected. Cessation of smoking for a period of one month brought about clinical improvement in only 2 of this group. Both these patients showed a hyperacidity after tobacco smoking.

3 Tobacco smoking had no relation whatsoever either to the subjective symptoms or to the clinical findings in the 6 patients with carcinoma of the stomach. The withdrawal of tobacco in no manner altered their subjective symptoms.

4 The 2 patients who were under observation and who had been operated on for ruptured duodenal ulcer showed no change in their gastric secretory findings after tobacco smoking. One of these patients had frequent heartburn which was relieved after cessation of smoking, but the pain which occurred between meals was entirely unaffected.

5 Of the 17 patients who had a gastro-enterostomy performed for duodenal ulcer it was difficult to determine any acid values after tobacco smoking because of regurgitation of intestinal

contents. The withdrawal of tobacco in 7 of these patients who had active clinical symptoms brought about an improvement in 3.

Excluding the 6 patients with carcinoma of the stomach, there were 94 adults with organic gastric disease. Approximately half of them presented themselves because of clinical symptoms and gave an associated history of tobacco smoking for a period of from five to thirty years. The active symptoms either disappeared or were ameliorated in about 80 per cent of this entire group, under proper medical management. In the remainder, despite medical treatment, there was persistence of symptoms, and it was not until tobacco was entirely withdrawn that active symptoms began to disappear and improvement followed. Some of these patients because of hunger pain would smoke, and although they had temporary improvement, occurrence of pain of greater severity would follow in a short time. With the relief of symptoms after tobacco had been withdrawn and comfort restored, the smoking of a few cigarettes was sufficient in some of these patients to bring about a return of symptoms. Apparently these individuals had become so sensitized to tobacco that they could not tolerate even the smallest quantity. In some patients smoking would cause a loss of appetite, and perhaps the pain could be ascribed to the fact that food was taken at very irregular intervals.

In order to obtain more definite data on the gastric motor and gastric secretory response to tobacco smoking, 50 patients of Group A and 50 patients



of Group B were studied more intensely

From Group A were chosen 10 patients from each of the five subgroups. These patients were all fluoroscoped on several occasions. The first fluoroscopic examination was made with the patient fasting so that data might be obtained as to the normal tone, peristalsis, size, shape, and position of the stomach. During the second examination the individual was allowed to smoke shortly after the barium meal was given. The blue light was on during this examination, so that the individual might see the smoke. Many of the patients did not enjoy smoking in the dark, and in order to have as normal a condition as possible, some light was allowed in the room. The third fluoroscopic examination was made after the individual had smoked on a "fasting" stomach and prior to the administration of the barium meal.

Fluoroscopic examination of the 10 patients selected from the group designated as having a probable gastritis showed a very little change either in the tonus or in peristaltic activity, whether the individual smoked before or after the barium meal was given. In the 10 patients chosen from the group designated as "gastro-cardial," smoking prior to the administration of the barium meal caused an increase in gastric tonus and in peristalsis in 2 of these patients. In 3 there was a decrease in tonus and in peristalsis if smoking were allowed after the barium meal was given. In the remaining 5 no change was observed at any time.

Peristaltic activity and gastric tonus was definitely increased in 22 of the

remaining 30 patients. These individuals had the most pronounced clinical symptoms in the groups designated as heartburn, "duodenal ulcer symptom-complex," and gastrospasm. Smoking prior to the administration of the barium meal produced a more marked gastric response than if smoking were allowed after the barium meal. On both occasions, however, there was an increase of peristalsis above the normal. In none of these patients was there any delay in the gastric emptying time. The increase in peristaltic activity would last from ten to fifteen minutes and then the contractions would decrease and become normal, and in some patients distinctly weaker than normal.

Danieleopolu and his co-workers report that in their studies x-ray examination showed a tendency to paralysis of the contracting power of the stomach starting ten to fifteen minutes after the first inhalation of smoke and persisting over an hour. This paralysis was often preceded by a phase of hypercontractibility and occurred with large amounts of tobacco smoke. It is assumed that small doses may stimulate the contractibility.

In studying the gastric secretory changes in these 50 individuals fractional analysis was done in the usual manner so that a curve for each was obtained. In those patients who showed a hyperacidity or a sub- or anacidity, fractional study was repeated to corroborate the primary findings.

In the 10 patients selected from the group stated as having a probable gastritis, smoking prior to the test meal study showed practically no change in

the acid findings, other than a slight increase in the amount of "fasting" gastric secretion. If the individual smoked one hour after the test meal had been given there was a slight increase in gastric acidity, but no distinct rise and practically no change in those patients who had a subacidity.

In the 10 patients selected from the group designated as "gastro-cardial," tobacco smoking prior to the giving of the test meal showed an increase in secretion, but no increase in acidity. When smoking was allowed after the test meal had been given in 6 of the 10 patients there was a decrease in gastric acidity which started within fifteen minutes after smoking was allowed and lasted during the entire study.

In the remaining 30 patients of this group (functional), after their normal gastric curves were obtained they were permitted to smoke prior to the giving of the test meal and one hour after the meal had been given. The duodenal bucket was in the stomach during the entire examination. Smoking prior to the test meal caused an increase in gastric secretion in one-half of this group. In about 20 per cent of this number there was an increase in acidity during the first hour, but in the second the gastric curve was similar to the normal one. If smoking was allowed one hour after the test meal was given, there was a distinct rise in figures above normal in about one-third of the entire number. Tobacco smoking at the end of the second hour period would again produce an increase in secretion, although the acid figures did not rise. These tests were repeated on several occasions and the chemical

findings were practically the same at all times.

Many brands of cigarettes were used in this group, including some of the alleged nicotine-free products, and there was practically no change in the findings.

It is of interest at this time to call attention to the findings of Bailey and his coworkers in their studies on "denicotinized" tobacco. According to their results, "denicotinized" products vary considerably in nicotine content. As a group, these products were found to contain less nicotine than tobacco, but practically all contained varying amounts, some even containing as much nicotine as is found in ordinary tobaccos. The results of their investigations are important for the reason that some individuals who are advised to discontinue tobacco smoking substitute these "denicotinized" products and may equal or exceed their usual consumption of nicotine. Frank also found approximately as much nicotine in alleged nicotine-free products as in normal tobacco.

The 50 patients chosen from Group B all had definite evidence of duodenal ulcer. The patients were males between the ages of 25 and 45 who had had symptoms for two or more years and had been smoking for at least five years.

Fluoroscopic study was first made to determine the tonus, peristalsis, and motor activity so that a conception of the normal activity of each stomach might be obtained. Many of these examinations were repeated to confirm the original findings. About one-half of the entire number were in the

quiescent stage, but all the patients were under medical supervision.

If fluoroscopic study was made after the individual had smoked on an empty stomach, there was an increase in peristalsis and in tonus in 10 per cent. of the entire group. Three patients had a paradoxical residue (Haudek) after four hours, which did not occur when the control study was made. Smoking one-half hour after the barium meal did not alter the peristalsis, although there appeared to be slight increase in tonus.

In order to study the secretory changes which occur after tobacco smoking, at least two fractional analyses were done on each patient prior to the tobacco test. Seventy per cent. of the group showed the usual acid curve for duodenal ulcer as described by Rehfus. There was a distinct increase of gastric secretion with high acid figures on the fasting stomach in 60 per cent of the group. If the patient was permitted to smoke prior to the giving of the test meal, there was an increase in the amount of fasting content. Fractional curves of test meal studies, after smoking was permitted on an empty stomach, showed a higher curve during the first hour with findings similar to the original studies during the second hour. If smoking was allowed at the end of one hour after the administration of the test meal, there was slight increase in acidity, and in a few instances there was a decrease in the acid figures. If the individual smoked at the end of the two-hour period, there occurred in about half the number a definite increase in the amount of gastric secretion and in the acid values. This lasted for about one-half hour. Three of

the patients on repeated study showed a decrease in acid values after tobacco smoking, whether allowed to smoke prior to or one hour after the test meal was given.

Most of the patients studied in both groups were cigarette smokers. Approximately one-fifth of the number smoked cigars only, some smoked cigars and cigarettes, and very few smoked a pipe. The technique of smoking and the individual sensitiveness to nicotine varies greatly and undoubtedly accounts for many of the gastric disturbances and for the fact that not all tobacco smokers are affected alike. Gastric symptoms and findings will depend upon whether or not one is a dry smoker, on the amount of tobacco which reaches the mouth, on the question as to whether or not one is in the habit of chewing the end of a cigar, and as to whether or not particles of the tobacco are swallowed. A great deal of nicotine usually collects in the stump of a cigar, and if the lower one-third of the cigar is not smoked, less nicotine will be burned and less will be absorbed.

On history taking it is, therefore, important to note not only how much, but also the art and manner of smoking. Although tolerance is easily acquired and habitual users may tolerate as much as 40 milligrams a day, the measurements of the amount of nicotine retained in the smokers, either swallowed or absorbed, vary greatly.

Gastric response to tobacco smoking may be due either to the action of nicotine on the ganglion cells in the gastric wall or to the action of nicotine (when swallowed with the saliva) directly on the gastric epithelial cells or

may be secondary to gastric blood-vessel changes due to the action of nicotine

### Conclusions —

1 Tobacco smoking should be considered an etiological factor in gastric functional disturbances

2 Individual sensitivity, rather than the amount of tobacco consumed, appears to be the determining factor as regards symptomatology

3 Gastric secretory and gastric motor response in individuals with functional gastric disturbances due to tobacco smoking vary, despite the similarity in clinical symptoms

4 Approximately one-fourth of in-

dividuals with gastric functional disturbances attributable to tobacco smoking show a hyperacidity, and about one-fifth a subacidity

5 In peptic ulcer tobacco smoking usually causes an increase of gastric secretion during the fasting stage, and a hyperacidity in about one-third the number

6 Clinical improvement in some of these patients with ulcer occurs only after cessation of smoking. The withdrawal of tobacco in these patients is most advisable

7 The therapeutic test, and not the chemical and roentgen findings, is the criterion as to whether or not the individual should smoke

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## Editorial

### *POST-VACCINATION EN- CEPHALITIS*

During the month of July of this year, much attention was given in the British press to comments upon deaths from encephalitis following vaccination, and to issues of great public importance thereby raised. Two of the cases arousing particular interest occurred in a girl aged fourteen and in a boy of twelve years, the first dying one month after vaccination and the second three weeks after. Both had symptoms of encephalitis developing on the 10—13th day after vaccination, and in both the autopsy examination of the brain and cord showed lesions characteristic of "post-vaccinal encephalomyelitis." There was nothing in the evidence to indicate anything abnormal about the method or the course of the vaccination, the coroner's verdict stating that there was no suggestion in the evidence that the vaccination had been otherwise than properly and skilfully carried out. The coroner's verdict in each case was "Death by misadventure." Commenting further, the coroner stated that this was the third case of the kind he had investigated within the last month, and that it is "disquieting to think that these cases are occurring more frequently than formerly. It is also disquieting to think that however careful one may be in the preparation of the lymph and in the methods of administration, this

disease may occur from time to time. Very little is known of this condition."

Commenting upon the case under question the pathologist, Professor H. M. Turnbull, stated that the occurrence of postvaccinal encephalomyelitis was now recognized generally to be connected in some way with vaccination. This connection was first shown in the London Hospital in 1922. It was recognized in Holland in 1925, and since then has been found in nearly every country. It was not considered by him to be a new disease, although apparently becoming more common. It had not been found that the disease was due to any fault in the preparation of the lymph or to any contamination. The exact cause had not yet been discovered. Some considered that this disease was due to the vaccinal lymph itself acting on persons who were abnormally sensitive to it. Most investigators believed that the vaccinal lymph lighted up infection which was lying dormant in the patient. The latter view had support in the observation that a very similar inflammation might complicate measles. All authorities are agreed that the disease has nothing to do with encephalitis lethargica or infantile paralysis. The illness is usually well defined on the 10th to the 13th day after vaccination. It may begin earlier or a little later. It has never begun months or years after vaccination. The disease may occur in infants under one year of age. When

all vaccinations are taken into consideration this complication of vaccination is extremely rare. According to the report of the Committee on Vaccination, Ministry of Health, 1928, there were 62 cases between October, 1922, and December, 1923, inclusive, approximately one case in 16,903 vaccinations. Very few of the reported cases were confirmed by microscopic examination. The great majority of cases had not been vaccinated before. In one of Turnbull's cases, there was a history of a previous vaccination but no scars of a successful take. "About half of those affected die, but the remainder, with few exceptions, recover completely."

In the "League of Nations" report on the subject, it is stated that "in our present state of knowledge, we must conclude that postvaccinal encephalitis is a different disease from encephalitis lethargica. The conditions under which postvaccinal encephalitis has manifested itself in the Netherlands and in England and Wales tend to show that children between 3 and 13 years of age are particularly susceptible, while infancy (disproved by Turnbull) and adult ages are almost wholly exempt. All observations point to the conclusion that the appearance of encephalitis is not connected either with particular strains of lymph, or with particular accidents of lymph preparation."

Passing to the etiologicopathological side of the problem, it would appear that in our present state of knowledge the virus of vaccination of itself cannot be considered responsible for the supervention of encephalitis. Rather it is to be supposed that some unknown factor exists—perhaps bacterial or a

filtrable virus, or a latent virus which by means of a reciprocal reaction determines the occurrence of the accidents in question.

The Report of the Committee on Vaccination, of the Ministry of Health, headed by Sir Humphrey Rolleston, issued in 1928, is an elaborate work of 322 pages with many charts and tables, in which the whole subject of diseases of the central nervous system following vaccinations is thoroughly analyzed. During November and December, 1922, there occurred amongst those recently vaccinated in and around London a few cases of an acute nervous disease of uncertain nature. Attention was first called to this in December, 1922, when four cases of the kind were admitted to the London Hospital, all of them fatal. In each instance there was a history of recent vaccination, and Dr. Turnbull, the Pathologist to the Hospital, was led to consider the cases as possibly associated with the vaccination on account of an apparently similar instance which had come under his observation in 1912. As a result of further inquiries a total of 11 cases, including the four above mentioned were brought to light in eight districts of the London area. These cases were, with one exception, primary vaccinations about the school age, and the period intervening between the onset of the illness and the vaccination ranged from 6 to 12 days. Seven of the cases were fatal, and the deaths were ascribed in 4 cases to polioencephalitis, in one case to acute anterior poliomyelitis and in 2 cases to meningitis. No similar cases were reported until the summer and autumn of 1923. During that period,

however, cases of acute nervous disease following vaccination were reported from various parts of the country, the onset of illness being usually 10 to 14 days after vaccination. These cases were widely spread, mainly in the southwest and midlands. For instance, there occurred at Tredegar what was thought to be a small outbreak of polioencephalitis affecting four children from 6 to 11 years of age. Three of them died, in these three the onset was 10 to 11 days after vaccination. In the fourth, which recovered, the interval was 12 days. At the time of these occurrences, smallpox was prevalent and vaccination largely increased in consequence. In London an unusually large number of persons were vaccinated. Similarly, in the summer of 1923, smallpox was again prevalent and a very large amount of vaccination and revaccination was going on. The cases of nervous disease coming to knowledge in this period were distributed to areas in some of which there had been a good deal of primary vaccination of children of school attendance age. Several other cases of nervous disease, fifteen in number were incidentally discovered during routine inspection duties by medical officers. Suspicion was aroused that the occurrences might be more widespread in distribution, and steps were therefore taken to ascertain whether similar cases were occurring generally throughout the country. The Registrar-General was asked to supply lists of deaths under 15 years of age from the following causes — Poliomyelitis, Polioencephalitis, Encephalitis Lethargica and Meningitis, (Tuberculosis and other

forms). Inquiry was then made in respect to every case in the lists, thus obtained in regard to the performance of vaccination within one month of the onset of the fatal illness. The Registrar-General's returns showed that during the months of July and August, 1923, 601 deaths at this age period were reported as due to one or another of the above causes. In these were only 10 cases in which vaccination had been performed within a month of the onset of the illness, and an analysis of these cases showed that the probable diagnosis in 3 cases was post-basal meningitis, in 5 cases tuberculous meningitis, and in 2 cases the diagnosis was obscure. These figures did not bear out the idea that any considerable portion of the deaths registered during July and August, 1923, due to meningitis and other diseases of the nervous system were associated with recent vaccination. The cases of encephalitis occurred in two groups separated by an interval of some six months, and in each the incidence of the disease was mainly confined to a very limited period. The first group of 11 cases occurred in London and its environs, and the dates of onset of the disease ranged from November 14th to December 15th, 1922, the cases having been vaccinated in the last nine days of November. Four of this series were examined histologically by Dr Turnbull. No other cases throughout England and Wales were reported at this time, but it was discovered later that on January 4, a case occurred at Colwall in Herefordshire. There were no further cases till the summer of 1923 when a second group arose consisting

of 50 cases. These occurred mainly in the provinces, most of them in the month of July. Of the 50 cases, one was vaccinated in May, 5 in June, 31 in July, 2 in August, 7 in September and 4 in October. Since the above, no other cases have been reported with the following exceptions. At Winsford, Cheshire, a man aged 45, who was vaccinated on February 9th, 1924, developed cerebral symptoms 13 days later, the condition being diagnosed as "Encephalitis lethargica", and in Birmingham in April, 1925, an infant who was vaccinated on April 6th, developed convulsions on the 15th, lost consciousness and died, the diagnosis being "Convulsions, meningismus following vaccination". There was an almost six months interval between the first group of cases and the second, and over a year has elapsed since the last case. During these periods vaccination has continued more extensively than usual, since smallpox has been prevalent to a considerable extent and over a wide area. Up to the date of this report, therefore, there were 64 cases which form its basis, two of these having been reported as the report was in press and are not included in this summary. Of 62 cases, there were 40 females and about 22 males, with an average age of  $10\frac{1}{2}$  years. In 7 cases, the ages ranged from 20 to 50 years. The mortality was 36 out of 62, or rather over 58 per cent. No direct proportional relation between the cases of postvaccinal encephalitis and the number of persons vaccinated was found to exist. The practitioners' diagnoses of the nervous symptoms from which 62 cases suffered showed great variation. The greater number of the

cases were attributed to meningitis, polioencephalomyelitis and its varieties, and encephalitis lethargica. In the area in which the cases occurred there was a high incidence of endemic poliomyelitis and polioencephalitis. In these areas vaccination was also much above normal. As to the lymph used, rabbit stocks predominated largely over calf stocks, the latter in fact being very few. The clinical data at the disposal of the Committee were in the majority of cases very scanty. These data suggest that the majority of the cases (47 out of 62) were alike and represent a homogeneous group. In most instances, the onset of symptoms was rapid and the course of the disease acute. The predominant symptoms were of cerebral rather than of spinal origin, and included fever, backache, headache, vomiting, strabismus and varying degrees of clouding of consciousness. Where paralysis of the limbs occurred, it was generally of the upper motor-neuron type. In other words, these cases, presented the symptomatology of encephalitis, indicating a diffuse inflammation of the brain, without special localization, and with very little evidence of involvement of the cord. Nine of ten cases, in which the after histories were followed up, recovered completely, without the paralyses which follow ordinary poliomyelitis or the mental or other disturbances which form the common sequelae of polio-encephalitis and encephalitis lethargica. One of the cases developed hemiparesis, probably permanent. None of the cases showed any complication as regards the vaccination process. In all, the course of vaccination appears to have



been normal and to have given rise to no undue constitutional disturbance, to no excess of local inflammation and to no septic invasion. There is, therefore, no reason to suppose that any marked debility occurred owing to the vaccination which might have led to a lowering of resistance. Postmortem records are available in six cases of the series. In all there was some degree of meningeal congestion, usually slight, and in one case there were slight meningeal hemorrhages. A little meningeal thickening was noted in one case, with some edema, and minute nodules which proved on section not to be tuberculous in character. The brain itself was found congested, the blood vessels conspicuous, in most cases, hemorrhages were noted in the nervous tissue, chiefly about the blood vessels. Softening of the brain was absent. In the spinal cord, marked softening was noted in one case, and local blurring of the pattern of the gray and white matter in another. Otherwise the changes were similar to those seen in the brain, namely, congestion and punctiform hemorrhages. The changes in other viscera were slight. The histological appearances were those of a diffuse encephalomyelitis, or meningo-encephalomyelitis. The nervous tissues showed a small celled infiltration of perivascular distribution. The perivascular sheaths contained lymphocytes, with larger cells having a large clear nucleus, possibly endothelial in nature. Polymorphonuclear leucocytes and plasma cells were less common as a rule, but in certain cases were well defined. In the parenchymatous foci the predominant cells had a large, clear, somewhat

irregular nucleus, and many were possibly derived from the neuroglia, lymphocytes were less abundant than in the perivascular sheaths. In these foci, which have an edematous appearance, chromatin fragments were also present, derived from cells which have broken down. Actual destruction of the neurones was rarely seen. As a rule the nerve cells still showed Nissl granules. Nevertheless, chromatolysis was often present, and on careful search more severely damaged neurones were found. Capillary hemorrhages occurred, but were infrequent and slight. Hyaline thrombi were not uncommon and were often associated with edema of the surrounding tissues. The data brought before the Committee suggest that the encephalomyelitis which followed vaccination in the cases under review was due to infection with a virus belonging to the group of neurotropic "filter passers." The essential problem is the relation between the cases of encephalitis under review and vaccination. Three possibilities suggest themselves. In the first place, it is possible that the cases of encephalitis were genuine sequelae of vaccination, and due solely to the virus of vaccinia. The second possibility is that the cases of encephalitis, though coincident with vaccination, were due to some different and independent cause. The third possibility is that the cases of encephalitis were due to the combined action of two morbid vira, viz, vaccinia and some other familiar or unfamiliar virus. In the majority report of the Committee, it is stated that there would appear to have been in the cases concerned something more than mere overlapping in time of vaccination

with some familiar or unfamiliar neurotropic virus, and that the unusual clinical and histological manifestations and lethal character of the best studied cases suggest that a combination of *vira* was operating. In the minority report made by Dr McIntosh he states that the histological and pathological appearances of the fatal cases are uniform and present an entirely new picture and that he is strongly of the opinion 'that we have had to deal with a hitherto undescribed inflammatory lesion of the central nervous system'. He considers vaccination to have been a casual factor and not a mere coincidence, and that the infection was either introduced by vaccination or that vaccination made the central nervous system susceptible to it. From 1923 to 1927, 124 cases of postvaccinal encephalitis occurred in Holland. The incidence of the disease in Holland during 1927 and the first half of 1928 has been estimated at one case per 2800 vaccinations. Public opinion in that country has been turned against compulsory vaccination. Towards the end of 1927, compulsory measures were suspended and in 1928 there were only 52 683 vaccinations as against 173,672 in 1926 and 150 653 in 1927. This suspension will continue until the end of the present year. The fact that practically all the cases of encephalitis followed the use of rabbit lymph suggests the possibility of infection with 'rabbit encephalitis', which is extremely common in American laboratory rabbits. The virus of this infection may be carried over in the lymph used for vaccination, and may possibly produce an encephalitis in susceptible children. Apitopos of the

use of rabbit lymph the following questions were put to the Minister of Health in the House of Commons in July. "When rabbits first began to be used in the production of government lymph supplies, whether any cases of post-vaccinal encephalitis were reported in this country prior to such introduction of rabbit lymph. Whether his medical advisors have considered the advisability of dispensing with the use of rabbits for the purpose in question. Whether he is prepared to guarantee that any child or person vaccinated with government lymph will not be seriously injured by the operation, and, if it is not possible, whether he will consider the desirability of introducing legislation to secure that compensation shall be given to the parents or dependents, as the case may be?" Until the question of etiology is settled the use of rabbit lymph should be stopped. Since Wilson and Ford have reported four cases of postvaccinal encephalitis in America, this disease becomes a matter of importance to us in this country, and steps towards its prevention should be taken by those concerned in vaccination. The unfortunate result of the situation is the ammunition afforded the anti-vaccinationists who have seized upon the occasion to further their cause against compulsory vaccination. It is, therefore, highly desirable that the problem of the etiology and prevention of post-vaccinal encephalitis be investigated at once by intensive research. A quick solution of this question is necessary for many reasons, the most important of which is the prevention of an anti-vaccination stampede, which resulting great increase in the incidence of small-pox.

## Abstracts

*Attempted Production of Vaccinal Encephalitis in Rabbits with a Testicular Virus*  
By RICHARD THOMPSON (Proc Soc f Exper Biology and Medicine, 1929, XXVI, p 559)

The reproduction of vaccinal encephalitis in rabbits is of interest at this time chiefly in view of the prevalence of postvaccinal encephalitis in some European countries. The possible use of the rabbit's brain as a medium for mass production of sterile vaccine (advocated by Levaditi) also adds importance to the question. A considerable number of European workers have succeeded in producing what they regard as a vaccinal encephalitis in rabbits. Levaditi and his co-workers since 1921 have developed a strain of vaccine virus known as neurovaccine which produces regularly on intracerebral injection into rabbits a typical encephalitis with paralytic symptoms and death in 4-7 days. They regard it as a virus adapted to the central nervous system by passage and consider that it has acquired neurotropic properties. They first adapted it to the brain by alternate brain and testicular passage, later omitting the testicular passages. Blanc and Caminopethos found that ordinary calf vaccine passed through the rabbit's cornea and then to the brain was sufficiently adapted to cause a fatal encephalitis. Herzberg produced a vaccinal encephalitis by the intracerebral injection of a virus adapted to the rabbit's testicle. The great majority of workers, however, have found no adaptation necessary and consider the encephalitogenic property as one inherent in ordinary vaccine virus. Marie, Krumbach, Condrea, Bachman and Bigliere, Burnet and Conseil, and Winkler have all succeeded in producing an encephalitis by the intracerebral injection of ordinary calf vaccine lymph purified by various means. Krumbach found no difference between calf lymph and lapine (vaccine adapted to rab-

bit's skin by passage). Condrea was unable to detect any difference between the action of cutaneous and testicular virus in the brain—both producing encephalitis. Bachman and Bigliere used four strains of vaccine and one of variola and obtained identical symptoms with all, although the symptoms described by them differ markedly from the typical picture described by most other authors. They also found no difference between testicular and dermal virus. Burnet and Conseil found that chloral or opium injections increased the susceptibility of the brain. Ledingham states that ordinary vaccine virus requires no special adaptation to the brain to kill by intracerebral injection. Reports of failures to produce encephalitis by vaccine virus are comparatively rare. Calmette and Guérin injected virus intracerebrally from the fourth, but not the seventh day, but make no mention of any symptoms or fatal disease. Camus was unable to produce encephalitis in rabbits by the intracerebral injection of pure vaccine and on the basis of this and the difference between the skin lesions of ordinary vaccine and Levaditi's neurovaccine is inclined to regard Levaditi's product as a mixture of vaccine virus with some other unknown virus. Walthard could not produce encephalitis by the injection into one rabbit of virus deposited in the brain of another after corneal infection. There is no report in the American literature on the production of encephalitis by an ordinary strain of vaccine, either by direct injection or with any means of adaptation, although Levaditi's neurovaccine has been used by a number of workers. In view of this Thompson considered it worth while to endeavor to produce an encephalitis in rabbits by using a strain not known to be adapted to the brain. The virus used was the testicular strain adapted by Noguchi originally. Injection into the fourth ventricle was used

at first because of its simplicity and its very successful use with herpes encephalitis. Later only direct intracerebral injection was used. Testicles and brains for passage were ground up with sand and a twenty per cent suspension in saline made and centrifuged to remove coarse tissue particles. The presence of virus was tested for by intradermal injections. The strain of virus used when injected by either method did not produce in any animal a fatal encephalitis or even any symptoms which could not be ascribed to the mechanical effect of the injection. The virus was found to survive at least four days in the brain after intracerebral injection but only for twenty-four hours after ventricular injection, with ventricular injection and previous meningeal irritation by sterile broth attempts to adapt the virus to the brain by 24-hour brain to brain passage were negative. Virus present in the first passage brain had completely died out by the fourth passage and fourth passage did not revive it. Animals of the series allowed to live showed absolutely no symptoms. Brains of two animals, dying after ventricular injection, which contained same virus, produced no symptoms, when injected into other animals. With direct intracerebral injection attempts to adapt the virus by brain to brain passage at 7-day intervals were negative. Alternating brain and testicular passage, as used originally by Levaditi, was also without result. The virus could be kept alive apparently indefinitely by alternate brain to testicle transfer but no evidence of any acquirement of intracerebral pathogenicity could be detected and if the testicular passages were omitted the virus soon died out. In conclusion, the strain of virus used is definitely not encephalitogenic for rabbits, if it can be made to produce encephalitis it can do so only with extreme difficulty. In view of the apparent ease with which many European workers have succeeded in producing encephalitis with an ordinary strain of vaccine virus, and the lack of positive or negative reports of any such attempts in this country, this failure to obtain a vaccine encephalitis in rabbits is considered of interest. An explanation which offers itself is that the power to pro-

duce encephalitis depends upon the strain of virus, some strains producing it readily, some only after adaptation and some not at all. The theory of Camus that a virus which causes encephalitis is contaminated by some unknown virus must also be held in mind. (Note by Editor. This work of Thompson's is of great value apropos of the present excitement in Europe over post vaccinal encephalitis. The editor believes that the theory of Camus of a vaccine virus contaminated by a neurotropic virus is most probably the true explanation of the encephalitis-producing vaccine virus. As suggested in the editorial in this number, may this unknown neutropic virus not be the agent of spontaneous rabbit encephalitis, which carried over with rabbit lymph may produce encephalitis in susceptible human beings? Levaditi's experiments can be explained on the grounds of a coincident infection in the rabbits with encephalitis. The possibilities of a relationship between rabbit encephalitis and post vaccinal encephalitis constitute a problem for which there should be a speedy solution sought.)

*Local Microscopic Changes Following the Administration of Antisyphilitic Drugs* By O. M. GRUHZIT (Arch. of Derm. and Syphil., June, 1929, p. 922)

Gruhzit has studied the pathologic changes produced at the point of injection in animals of the main types of antisyphilitic drugs. From this study it appears that the administration of the arsphenamine type of drugs intramuscularly invariably results in the formation of sterile abscesses, the healing of which is slow. At the end of eight weeks the healing has shown little progress. In this respect, sulpharsphenamine causes just as extensive an injury as neoarsphenamine. The mercury compounds produce the same type of injury only in a lesser degree. The injured areas, however, are more rapidly absorbed and fibrosed, especially when mercury thiobenzoate, benzoate and cyanide are used. The ultimate result is a scar tissue at the site of injection. The bismuth compounds cause local injury according to the degree of corrosiveness. The least injury is produced in the case of water-soluble compounds, such as bismuth thioglyco-

late The bismuth compounds suspended in oil or water cause considerable local necrosis, which is usually followed by the formation of a sterile abscess. The absorption of the necrotic material with the formation of a scar is a prolonged process. This, however, occurs more readily in the muscle under constant exertion than in an inactive muscle. Bismuth thioglycolate, a water soluble and tissue-soluble preparation causes the least injury to the tissues at the site of injection and is followed by a most rapid healing of the lesion. The tissue-fluid insoluble bismuth preparations must first be dissolved by the tissue fluids before they can be absorbed. Phagocytic action, if present, appears to be of minor importance.

*Prevention of Diabetic Deaths* ELLIOT P JOSLIN (Massachusetts Dept. of Public Health, June, 1929)

In a pamphlet distributed by the Massachusetts Department of Public Health, Joslin has set forth the diabetes mortality in that state, and the principles for the prevention of diabetic coma. Diabetes under the age of 20 has almost disappeared from the state, between the ages of 20 and 40 the mortality from the disease is lower than at any other time in this century, whereas above the age of 50 there has been a gradual rise. This rise does not begin for men until the age of 60, so that it is the women after the age of 50 who are chiefly responsible for the increasing death rate in Massachusetts. The diabetic mortality can be lowered still more provided the physicians of the state attack coma more efficiently. Out of 1044 fatal cases of diabetes reported to the Metropolitan Life Insurance Company up to April 15, 1929, coma was responsible for 433 deaths or 41 per cent. It is really the fault of the profession, says Joslin, that the mortality from diabetes is not decreasing, because diabetic coma is always preventable and nearly always curable. As one of the best practitioners in the state said recently, "Diabetes is a chronic disease, but doctors do not realize that it has acute manifestations." Indeed coma develops because of ignorance, negligence or carelessness. Diabetics go into coma carelessly because they break their diets and overeat, they go into

coma as a result of negligence when in the course of an infection, either general like measles or local like a boil, they neglect to make the proper tests to determine whether they are using enough insulin, they go into coma ignorantly, because they stop their insulin when they cease to eat for one cause or another. A diabetic should never omit his insulin unless his urine is sugar free. He must never forget that when he stops eating, he begins eating himself—his own body—and so still requires insulin, and often very much more insulin than before. If he has an infection as a cause of his loss of appetite he should know that an infection lowers the value of insulin and thus makes more insulin than usual a necessity. Coma and by diabetic coma, is meant acid poisoning, may steal away a diabetic before he or his friends suspect it. Within a few hours such mild symptoms as indigestion, lack of appetite, and pain in the abdomen may be followed by difficult breathing, drowsiness and unconsciousness. The only safe way for the diabetic to protect himself against coma is to keep well and sugar free all the time. Joslin tries to instill the following principles into the minds of every diabetic he sees. Whenever he feels ill and sick he should call his doctor, go to bed, take a hot drink every hour, take an enema, keep warm, get a nurse or someone to care for him. Another good rule is to have boiled water ready for the doctor when he arrives in case he wishes to use it. Promptness in diagnosis of coma is everything, and next to it comes energetic treatment at the earliest possible moment. If coma exists the doctor must give up everything else until the patient comes out of it. Insulin is usually required every half hour in 10-40 unit doses or more, varying with the severity of the symptoms, and if it is given intravenously it should always be given subcutaneously at the same time. Dehydration of the patient must be overcome by the subcutaneous injection of normal salt solution and one cannot rely on fluids given by the mouth or rectum. The heart is almost always weak and needs stimulation with caffeine sodiobenzoate,  $7\frac{1}{2}$  grains, and this may be given every hour if need be, for three or four doses. On

account of the weakness of the heart, salt solution must be injected very slowly if given intravenously. With children and usually with adults the stomach is distended and unless evacuated prevents the retention of liquids such as water gruels, ginger ale, or the juice of 2-3 oranges in other words, carbohydrate amounting to 50 grams. Therefore, the stomach should be gently washed out.

*Thrombo-Angitis Obliterans Experimental Reproduction of Lesions* LEO BUECHER (Arch of Path 1920 p 381)

In a paper published in 1914 Buerger expressed his conviction that the acutely inflamed veins and nodosities of thrombo-angitis obliterans could furnish the material in which an infectious agent-virus or micro-organism might reside and be brought to light second, that these foci might be utilized for the reproduction of the acute lesions of the malady. He has carried out investigations extending over ten or more years in the attempt to find a micro-organism. Failing in this effort he turned his attention to the reproduction of the acute lesions of the disease. He employed simple ligation of the veins of the fore-arm or arm for control purposes, he implanted or inoculated the coagulum of acute thrombo-angitis obliterans into the lumen of ligated veins, and implanted acute thrombo-angitis coagulum against the walls of ligated veins in man and monkeys. As a result, the paravascular implantation of clot from cases of thrombo-angitis obliterans was followed by the development of typical lesions of the disease in the apparently healthy ligated veins of the inoculated person. In two experiments on monkeys he failed to produce other than a bland thrombosis, a fact which would suggest that these animals may be immune. Other types of monkeys will be employed as soon as material becomes available.

*Studies of Experimental Streptococcus Arthritis IV Effect of Sodium Salicylate on Skin Allergy* R. A. KINSELLA and O. E. HACHBUSH (Proc Soc f Exper Biology and Medicine, 1929, XXVI, p 857)

The effect of sodium salicylate on the development of dermal allergy in the presence

of hemolytic streptococcal arthritis was studied because this drug is commonly employed in the treatment of acute rheumatic fever, and because the studies of Swift concerning the pathogenesis of this disease support the idea that allergy to streptococcus of various kinds is a factor in its production. As previously reported by these workers, the production of arthritis in rabbits by the inoculation into a knee joint of 0.1 cc of 24 hr broth culture of hemolytic streptococcus will be followed in 6 days by the appearance of a strongly positive local reaction to intradermal injection of a filtrate of a 5 days' culture in Harley's medium. The skin reaction takes 12 to 24 hours to develop. All rabbits were tested previous to the experiment and found to give no such reaction. Twenty-four rabbits were employed for this study, twelve of which received sodium salicylate, 6 received the drug for a considerable period before receiving an intra-articular injection of 0.1 cc of culture of hemolytic streptococcus, and 6 rabbits received the drug and the culture at the same time. The dose of sodium salicylate was 0.2 gm per kilo in 4 percent solution and was given intravenously. The first series of 6 received 8 daily injections of salicylate and after an interval of 12 days, during which the animals were in good health received 6 more injections given at 2 day intervals. After the injection of streptococci into the knee joint, 3 more daily injections of sodium salicylate were used, and 3 days later skin tests were made. At this time 3 of the series were dead. The 3 survivors showed completely negative tests. In the second series of rabbits the animals received the injection of salicylate 24 hours before the intra-articular injection was made. Thereafter 4 daily injections of salicylate were given and 4 animals survived. These gave completely negative tests. In the 12 control rabbits strongly positive skin reactions occurred 6 days after arthritis was produced and the reactions remained positive. The arthritis was highly fatal to all the animals but more so to those receiving the salicylate. The conclusion is supported, that the intravenous injection of sodium salicylate prevents the development in rabbits having a streptococcal arthritis of a positive skin reaction to filtrate of hemolytic streptococcus culture.

## Reviews

### *Principles and Practice of Electrocardiology*

By CARL J. WIGGERS, M.D., Professor of Physiology in the School of Medicine of Western Reserve University, Cleveland, Ohio. 226 pages, 61 illustrations. The C. V. Mosby Company, St. Louis, Mo., 1929. Price in cloth, \$7.50.

The use of the Einthoven string galvanometer by a privileged few has so thoroughly demonstrated its value in the diagnosis of heart diseases that a more general demand for electrocardiographic apparatus has been created. This increasing demand has enabled manufacturers of scientific apparatus to develop and market commercial models easy to operate and free from the inconveniences originally attached to the use of such apparatus. But unfortunately the training of medical men in the use of such apparatus and in the interpretation of electrocardiograms has not kept pace with this demand. Few courses in electrocardiography are included in under graduate or post graduate curricula of medical schools, so that opportunity for systematic instruction is decidedly restricted. It is obvious, therefore, that a more general self-training of physicians in the principles and practice of electrocardiography must take place. The need of a simple yet comprehensive treatise by an author who can reasonably lay claim to experience, both in the use of such apparatus as well as in the didactic presentation of this particular subject, is therefore apparent. This book is written with the object of filling this need. It is based on the author's practical experience in giving courses in electrocardiography in the medical schools of Cornell University and of Western Reserve University. The book is divided into three sections. The first deals with the general principles and procedures of electrocardiography, with the physics of the galvanometer and accessory systems, and on the basis of such knowledge, passes on to a considera-

tion of the operation of different models. The second part explains the cause of the normal electrocardiographic deflections and their relation to physical and physiologic processes in the heart. It then proceeds logically to an analysis of abnormal cardiac disturbances and their effects on electrocardiograms. The third section considers a series of abnormal electrocardiograms from patients which are presented as unknowns. It points out the evidences of abnormalities in each, discusses their significance in terms of clinical physiology, and thus arrives at a diagnosis. This is followed by a brief discussion of the salient features of the disorder studied, and of the treatment which has been given the stamp of approval. Experience has shown that in this way all the more common abnormalities can be presented in an interesting fashion and a method for the scientific evaluation of other records is taught. This is a very complete survey of the subject, and an indispensable book for the internist. It is well written in a clear concise style, and sufficiently illustrated. It is an important addition to the literature of electrocardiology.

### *Clinical Laboratory Methods*

By RUSSELL LANDRAM HADEN, M.A., M.D., Professor of Experimental Medicine, University of Kansas, School of Medicine, Kansas City, Kansas. Third Edition. 317 pages, 69 illustrations and 4 color plates. The C. V. Mosby Company, St. Louis, Mo., 1929. Price in cloth, \$5.00.

This manual was written originally to provide a simple yet complete outline for the average clinical laboratory worker. Only such methods were described as had proved both practical and dependable. Certain procedures which are seldom used, such as the qualitative determination of acetone bodies in the urine, have been omitted. Other methods have been revised. The one most im-

portant addition is the technic for the Kahn precipitation test for syphilis. A few entirely new methods, such as the determination of indican in blood, have been added. A survey of this edition lends us to note many important omissions. For instance, the only method for the staining of spirochaeta pallida given is one employing Wright's blood stain, a method which does not compare with the silver nitrate cover-glass methods. Methods are given for the staining of connective-tissue fibers, tubercle bacilli in tissue and Gram-positive bacteria in tissue, but no method is given for the staining of spirochaeta pallida in tissues. Surely the demonstration of spirochetes of syphilis in tissue sections is among the most important, but most neglected, functions of the clinical laboratory, and a book on clinical laboratory methods which omits these cannot be said to be complete. Further, the laboratory diagnosis of Tularemia and Malta Fever is not even mentioned. This book cannot be considered as up to date.

*Textbook of Clinical Neurology*. For Students and Practitioners. By M. NUSTADTER, M.D., Ph.D., Visiting Neurologist, Central Neurological Hospital, Welfare Island, Clinical Professor in Neurology, New York Polyclinic Medical School and Hospital, Outpatient Department Stuyvesant Polyclinic, St. Mark's Hospital, Neurologist King's County and City Hospital, Welfare Island, New York. With an Introduction by EDWARD D. FISHER, M.D., Professor Emeritus of Neurology, University and Bellevue Hospital Medical College, New York. 602 pages, 228 illustrations, some in colors. F. A. Davis Company, Philadelphia, 1929. Price in cloth, \$6.00.

This book is written primarily for the medical student and general practitioner rather than for the neurologist. In writing it, therefore, it has seemed wise to depart from the classical arrangement and to present the material according to its actual occurrence in medical practice. The general practitioner or the student at the patient's bedside hears a story and sees symptoms. Not being a specialist in the field of neurology, he is not likely to recognize whether

the symptoms found relate to disturbance of the brain, cord, peripheral nerves, muscles or endocrine glands. Consequently the first thing looked for, in consulting a reference book, is symptomatology, and in the usual textbook the arrangement of the book forces him to search from chapter to chapter. In order to save time the student and general practitioner require a working knowledge of the subject of neurology in as concise, lucid and complete a manner as possible. The author has been frequently importuned by his students to write a book of this type, a sort of *vade mecum*. This book is the result. Its principal theme is the semiology of the disorders of the nervous system. Symptom complexes found at the bedside or in the consultation room, constitute the chapter divisions. Under these are discussed the various diseases exhibiting such syndromes and their relationship to the structures affected—nervous, endocrine, muscular or osseous, as the case may be. Thus, the description of diseases begins with symptoms, and after the symptoms have been fully described, etiology and pathology, diagnosis, prognosis and treatment are taken up in the order named. It should be emphasized that the material of this volume is based mainly upon the author's personal clinical and pathological experience during the last twelve years. He has made a special effort to be brief and lucid, yet to incorporate all the material facts without befogging the issue. In this he has been unusually successful. Especial attention has been given to the subject of poliomyelitis and epidemic encephalitis. The tremograms devised by the author also constitute a novel feature of the book. The illustrations are abundant and for the greater part very good. Altogether this book is to be recommended as a valuable adjunct in the study of neurology.

*The Common Head Cold and Its Complications*. By WALTER A. WELLS, A.M., M.D., F.A.C.S., Professor of Oto-Laryngology, Georgetown University, Washington, D.C. With an introduction by HUGH S. CUMMINGS, M.D., Surgeon General, United States Public Health Service. 225 pages, 15 illustrations. The Macmillan Company, New York, 1925. Price in cloth, \$2.75.



According to a survey made by the Public Health Service, there is, on account of colds in the United States, an average annual loss of work of about two and one-fifth days for each worker, so that taking into consideration only that part of our population engaged in industry, which is about forty-two million, there may be estimated a loss of more than ninety million work days per year. Rendered in terms of money this means a loss of not less than four hundred and fifty million dollars every year on account of colds alone. This, however, by no means represents the total economical loss of colds, for it does not take into consideration the loss in energy and efficiency for many days following an attack, the loss from illness indirectly due to colds, or the cost of medicine and medical and nursing services. There can be no doubt that the unrestricted occurrence of the common head cold seriously affects the health, happiness and efficiency of the human race. Are colds contagious? Are drafts harmless? Do vaccines prevent? Is the use of spray and gargles advisable? Ought adenoids and tonsils to be removed? Is sinus inflammation curable? These are some of the vital, pressing questions, upon which enlightenment is demanded and urgently needed. The aim of this book has been to answer these questions, and to explain to what extent colds are dependent upon general health as well as local conditions. Included is a special discussion of the subjects of diet, clothing exercise, bathing and ventilation, which have a direct bearing upon the tendency to catch colds or the capacity to withstand them. The author believes that much can be done by judicious treatment of colds, which will not only tend to lessen the duration of the cold but to modify its course, to prevent complications and to forestall unfortunate consequences. There is included in the book a chapter dealing with home care and the general principles of home treatment, indicating these general measures to be followed, and these which are contrary to sound doctrine and therefore to be avoided, with instructions as to what the patient may safely do for himself and under what circumstances he should consult a physician to insure re-

covery. The complications of colds are considered in chapters on Adenoids and Tonsils, Sinus Disease and Voice Trouble. The author hopes that a rational up-to-date presentation of these topics may not be without value in dissipating some of the superstitious opinions and absurd practices that have ever clung to the subject of colds, which he believes is largely due to the indifference of the medical profession itself and its failure to instruct the general public in a matter of such great importance to health and happiness. Much useful information is contained in this little book.

*Handbook of Microscopical Technique For Workers in Both Animal and Plant Tissues*. Edited by C. E. McCLEUNG, Ph.D., Professor of Zoology and Director, Zoological Laboratory, University of Pennsylvania. 495 pages 43 illustrations. Paul B. Hoeber, Inc., New York, 1929. Price in cloth, \$8.00.

The book is divided into two parts. Part I outlines approved methods for the inexperienced worker and Part II for the experienced investigator. By a system of cross-reference between the two parts, all unnecessary repetitions are avoided. In Chapter I general methods are considered, in Chapter II methods for fresh material, in Chapter III bacteriological methods, in Chapter IV general botanical microtechnique, in Chapter V cytological methods, in Chapter VI embryological methods, in Chapter VII histological methods, in Chapter VIII protozoological methods, in Chapter IX fixation and fixatives are discussed, in X stains and staining, while Chapter XI is given up to a miscellaneous consideration. On careful examination this book proves to be a great disappointment. Instead of taking the place of the German *Encyclopedia of Microscopic Technique*, at least as far as the worker in pathology is concerned, the parts of this book that can be utilized by the practical pathologist are very slight indeed. No methods for the staining of spirochetes are given, and the special methods for the demonstration of hemosiderin, calcification, etc., are not included. The book is written from the standpoint of general science rather than from that of a practical pathological lab-

oratory. For this reason it will be of little use to the pathologist, with exception of the neuropathologist since neurological technique is more adequately presented. The same is true of botanical and general zoological technique.

*The History of Hemostasis*. By SAMUEL CLARK HARVEY, M.D., Professor of Surgery, Yale University, Surgeon in Chief, New Haven Hospital. 128 pages, 19 illustrations, Paul B. Hoeber, Inc., New York, 1929. Price in cloth \$1.50.

Another of the delightful little volumes on medical history from the house of Hoeber! Reprinted with additions and corrections from *Annals of Medical History*, N. S. Vol. 1, No. 2, March, 1929. In this *obitopus* in medical history the control of hemorrhage has been chosen as the thread to be followed amidst the varying fortunes of surgery. Beginning with the mention of the superstitious respect for blood held by primitive man and the attempts at hemostasis in the epics of early Greece and Rome the beginning of hemostasis in the early Medicine of Egypt, China, India, Assyro-Babylonia and Greece are described. The doctrine of the *pneuma* befogged the observations of the early anatomists. In the Golden

Age of Roman medicine, from Celsus to Galen, the theory of *pneuma* was dispersed, the knowledge of anatomy was furthered, and hemostasis progressed to the use of ligatures and styptics. The next step in hemostatic usage was the almost universal employment of the cautery, which lasted up to the time of Pare, who in 1564 advised the abandonment of the cautery and adopted the use of the ligature. In 1674, Morel was as far as can be determined, the first to use the tourniquet. This became the standard practice of the 18th century. Lister's part in the antiseptic ligation of vessels, the use of carbolized catgut, the application of an artery forceps and the casting about the vessel of a ligature bring the manipulations of hemostasis up to the practice of the present day. "The groping Alexandrian anatomist, the practical Greco-Roman surgeon, the consummate Pare, the obscure Morel, and the patient experimentalist, Lister, contributed the essentials, a host of surgeons provided the refinements." As a result, the operator of today may delegate to the background of the procedure that which for ages was an almost insurmountable obstacle, and proceed without fear of hemorrhage calmly and unhurriedly, in such a manner as to ensure for the patient all that surgeons still can provide.

## College News Notes

Dr Walter S Leathers (Fellow), Nashville, Dean and Professor of Preventive Medicine and Public Health, Vanderbilt University School of Medicine, has been appointed a member of the National Board of Medical Examiners to fill the vacancy made by the retirement of Admiral Edward R Stitt (Fellow), U S Navy, as Surgeon General

Dr T Homer Coffen (Fellow), Portland, Oregon, addressed the Portland City and County Medical Society, June 5, on "Misuses of Digitalis"

Dr Frank R Menne (Fellow), Portland, Oregon, addressed the Marion-Polk-Yamhill County Medical Society at Salem, June 4 on "Carcinoma of the Lungs"

Dr Christopher G Parnall (Fellow), Medical Director of the Rochester General Hospital, Rochester, N Y, was installed as President of the American Hospital Association at the recent annual meeting in Atlantic City, N J

Dr Henry Green (Associate), Dothan, Ala, was elected President of the Chattahoochee Medical and Surgical Association at its twenty-ninth annual meeting on July 10 Dr Green is a past President of the Houston County Medical Society and of the Medical Association of the State of Alabama

Dr Hugh S Cumming (Fellow), Surgeon General, U S Public Health Service, has been appointed by President Hoover to act on a planning committee to inaugurate a national investigation of the progress and present situation in the health and protection of childhood

The Florida East Coast Medical Association was addressed on June 14-15 by Dr Stewart R Roberts (Fellow), Atlanta, Ga, on "Jaundice"

The honorary degree of Doctor of Science was awarded to Dr James Allen Jackson (Fellow), Danville, Pa, during the recent commencement of Bucknell University

Dr Joseph McFarland (Fellow), Professor of Pathology, University of Pennsylvania School of Medicine, will become head of the new Cancer and Abnormal Growth Registry to be established in September at the Research Institute of the Lankenau Hospital, Philadelphia

Dr James B Herrick (Fellow), Chicago, emeritus professor of medicine, Rush Medical College, gave the commencement address at Lewis Institute recently

At the annual election of officers of the Chicago Medical Society, Dr James H Hutton (Associate), Secretary of the Society, was made President-Elect while Dr Nathan S Davis, III (Fellow) was elected the new Secretary

During the seventh annual assembly of the Twin Lakes District Medical Society at Rockwell City, Iowa, Dr Walter C Alvarez (Fellow), Associate Professor of Medicine, University of Minnesota Graduate School of Medicine, spoke on "Diagnosis of Gastro-Intestinal Disease", Dr Julius H Hess (Fellow), Professor of Pediatrics, University of Illinois College of Medicine, Chicago, spoke on "Diagnostic and Therapeutic Suggestions Covering Some Chronic Abdominal Conditions in Infants and Children", and Dr William W Duke (Fellow), Kansas City, Mo, spoke on

### "Allergy as It is Encountered by the General Practitioner"

The program of the fifty-first annual meeting of the Medical Association of Montana included addresses by the following Fellows of the College: Dr. Frederic W. Schlutz, University of Minnesota Medical School, on "Fundamental Factors Underlying the Development of Alimentary Disorders in Infancy and Childhood"; Dr. Harold W. Gregg, Butte, on "Epidemic Meningitis"; and Dr. Louis H. Flegman, Helena, on "Cancer Film."

Dr. Solomon Solis-Cohen (Fellow), Philadelphia, will be the Chief of Staff of the new Willow Crest Institution for Convalescents at Willow Grove, Pa.

Dr. Milton M. Portis (Fellow), Chicago, has been elected Clinical Professor of Medicine at Loyola University School of Medicine.

Dr. Virgil E. Simpson (Fellow), Louisville, recently addressed the Tenth District Medical Society at Winchester, Ky., on "Differential Diagnosis of Tumor of the Lung."

Dr. David P. Barr (Fellow), Professor of Medicine, Washington University School of Medicine, St. Louis, who delivered the commencement address at Central College, was awarded the honorary degree of Doctor of Laws, on June 5.

Dr. Everett K. Geer (Fellow), St. Paul, was one of the speakers, on June 15, at an afternoon meeting of the Southern Minnesota Medical Association on the Mississippi River near Winona.

Dr. Alfred Stengel (Master), Philadelphia, addressed the annual meeting of the medical alumni of the University of Pennsylvania on

Dr.  
Macon,  
was gr

tor of Public Health at the recent commencement of the University of Georgia.

Surgeon General Hugh S. Cumming (Fellow), Washington, D. C., was recently elected to honorary membership in the Delta Omega public health fraternity.

Dr. James L. McCartney (Fellow), Hartford, Conn., has been appointed chief of the department of mental hygiene of the Connecticut State Department of Health.

Dr. William A. White (Fellow), Washington, D. C., Superintendent of St. Elizabeth's Hospital, is Chairman of the Board of Managers of the Washington Institute for Mental Hygiene, which was incorporated on June 24. The Washington Institute for Mental Hygiene will open its first clinic in October.

Dr. Benjamin Goldberg (Fellow), Chicago, Secretary of the Board of Directors of the Municipal Tuberculosis Sanitarium, delivered the twentieth anniversary address at the Preventorium (Farmingdale), May 31, on the fundamentals of a national child health program.

Dr. Elliott P. Joslin (Fellow), Boston, was one of the speakers at the annual meeting of the Lake Keuka Medical and Surgical Association.

Dr. Lewis B. McBrayer (Fellow), Southern Pines, addressed the Third District Medical Society of North Carolina on "Organized Medicine."

Dr. Leroy H. Sloan (Fellow), Chicago, with the assistance of local physicians, held a Clinic at the Allen Memorial Hospital (Waterloo) on June 2nd, and in the evening addressed about twenty-five physicians from

Dr Edward D Spalding (Fellow), Detroit, delivered an address before the Me-costa County Medical Society (Big Rapids) on "Modern Cardiac Therapy"

Dr Samuel F Haines (Associate), Rochester, Minn., was one of the speakers at the thirty-second annual meeting of the Upper Peninsula Medical Society held at Ironwood (Michigan), August 7-8, his subject was "Early Diagnosis of Exophthalmic Goiter"

Dr David C Wilson (Fellow), formerly of the staff of the Clifton Springs Sanatorium, has been appointed Associate Professor of Psychiatry and Neurology of the University of Virginia Department of Medicine (Charlottesville)

Dr Peter Irving (Associate), New York, New York, has been appointed Assistant Secretary of the Medical Society of the State of New York

Dr L. R. Sante (Fellow), St. Louis, Missouri, is Professor and Director of the Department of Radiology, at the St. Louis University School of Medicine

Dr Harold Swanberg (Fellow), Quincy, Illinois, is Editor of "The Radiological Review"

Dr Judson Daland (Fellow), Professor of Medicine, University of Pennsylvania Graduate School of Medicine, has been assisting in the campaign against the tsetse fly in Africa during the past few months

Dr W McKim Marriott (Fellow), Dean and Professor of Pediatrics, Washington University School of Medicine, St. Louis, Presented a symposium on "Nutrition" during the twenty-eighth annual meeting of the American Society of Orthodontists, Estes Park, July 15-20

Dr Kenneth M Lynch (Fellow), Charleston, S. C., was made President-Elect of the American Society of Clinical Pathologists,

during its recent meeting at Portland, Oregon

Dr Stuart Pritchard (Fellow), Battle Creek, addressed the joint meeting of the Fulton County Medical Society of Ohio and the Lenawee County Medical Society of Michigan, on "Early Diagnosis of Pulmonary Tuberculosis"

Dr James M Anders (Master), Philadelphia, received the Degree of Doctor of Laws from Pennsylvania Military College, Chester, during its June graduation-day program

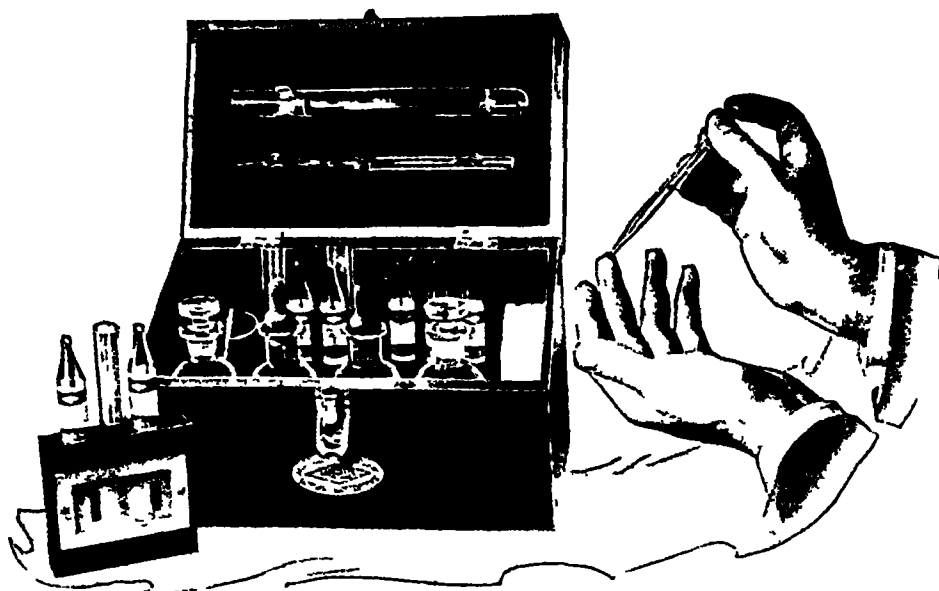
Dr Edward L. Bortz (Fellow), Philadelphia, is author of an article, "Viscerop-tosis," which appeared in the Journal of the American Medical Association, July 6, 1929

Dr Henry A Christian (Fellow), Boston, is the author of an article, "Nephrosis", a Critique, which appeared in the July 6th Number of the Journal of the American Medical Association

Dr Walter M Simpson (Fellow), Dayton, Ohio, was awarded the Ward Burdick Research Award (gold medal) at the recent meeting of the American Society of Clinical Pathologists, at Portland, Oregon, for his researches in tularemia and undulant fever. At the meeting of the American Medical Association at Minneapolis last year, Dr Simpson was awarded a gold medal for his exhibit of the pathology of tularemia

Dr A S Warthin (Master), has returned from England where he presented his work on syphilis before the British Medical Association at the Manchester meeting in July

In the 1928 Atlanta Proceedings of the Inter-State Postgraduate Assembly of North America there is published a survey of Dr Warthin's work on Cardiovascular Syphilis



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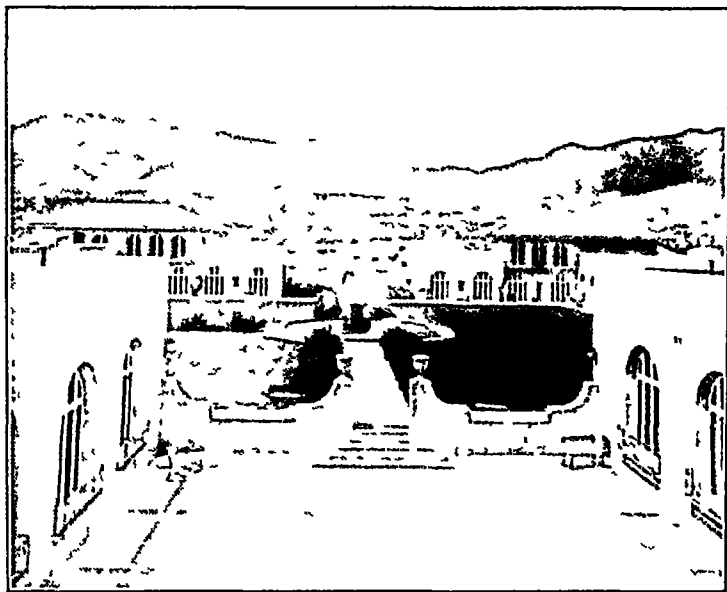
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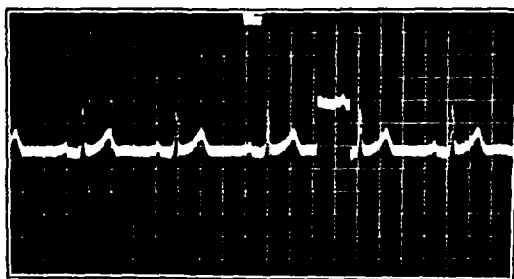
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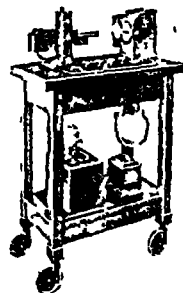
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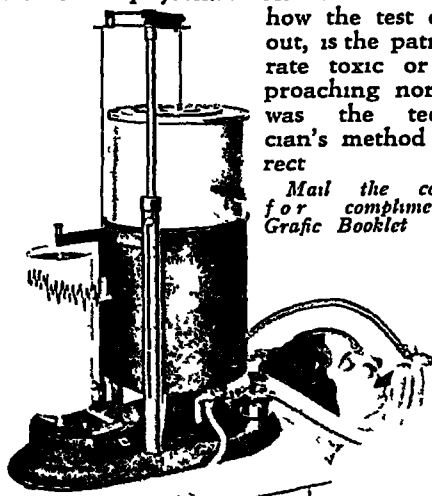
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The Journal will make an especial feature of the reviews of monographs and books bearing upon the field of Internal Medicine. Authors and publishers wishing to subject such material for the purposes of review should send it to the editor. While obviously impossible to make extended reviews of all material, an acknowledgment of all matter sent will be made in the department of reviews.

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ALDRED SCOTT WARTHIN, M D.  
Pathological Laboratory, University of Michigan  
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J. A. E. Eyster, B.Sc., M.D.

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Associate Physician, Wisconsin General Hospital



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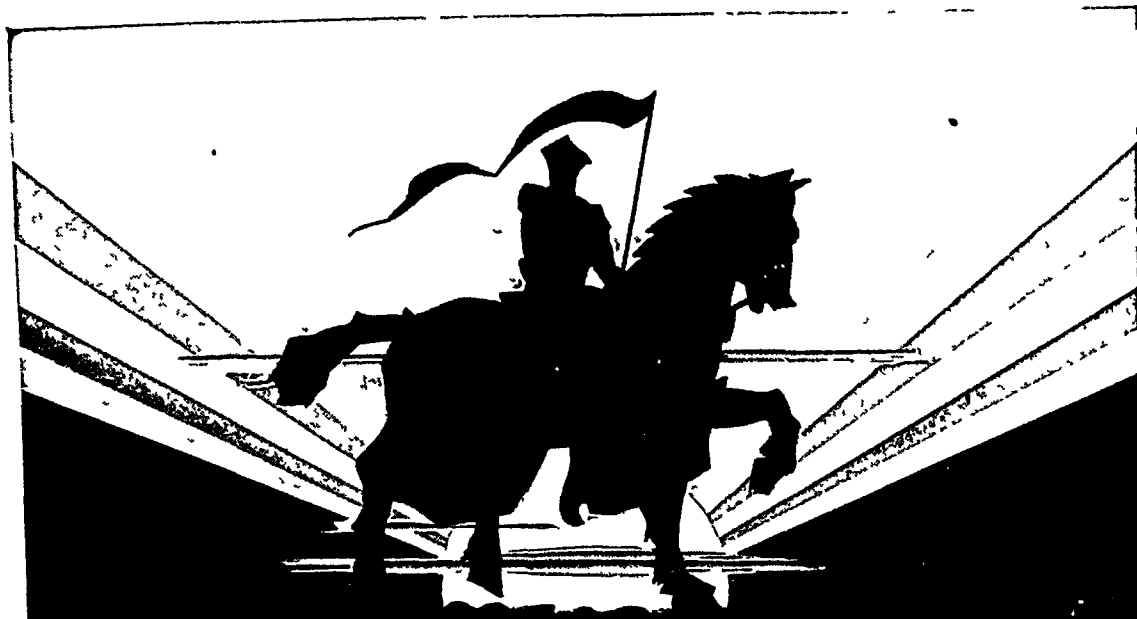
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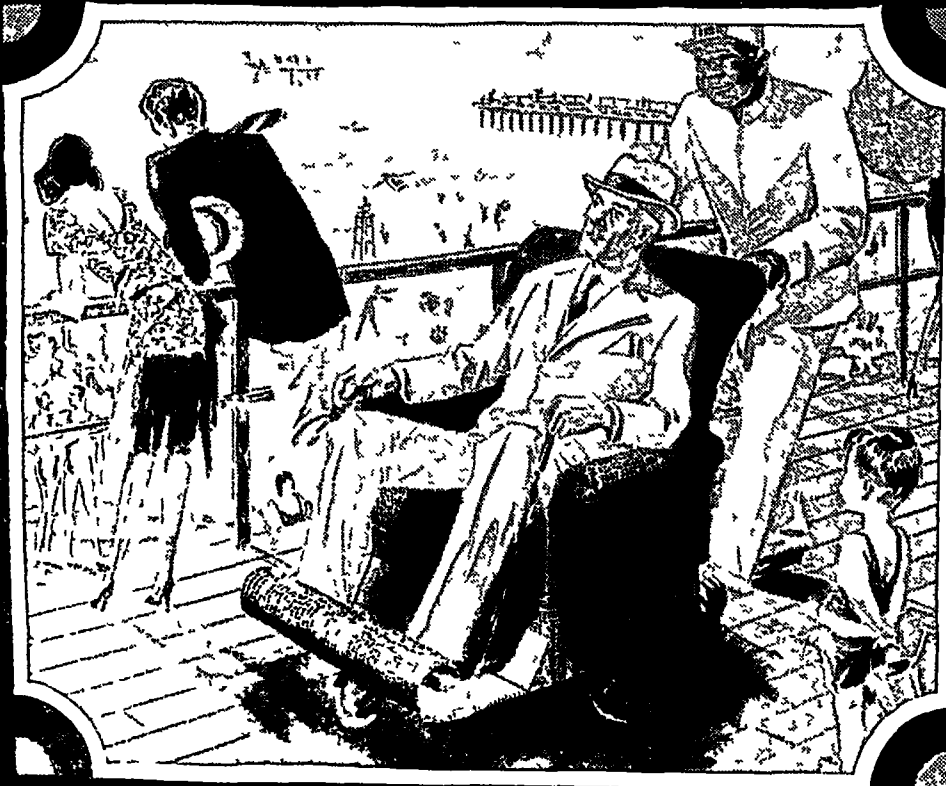
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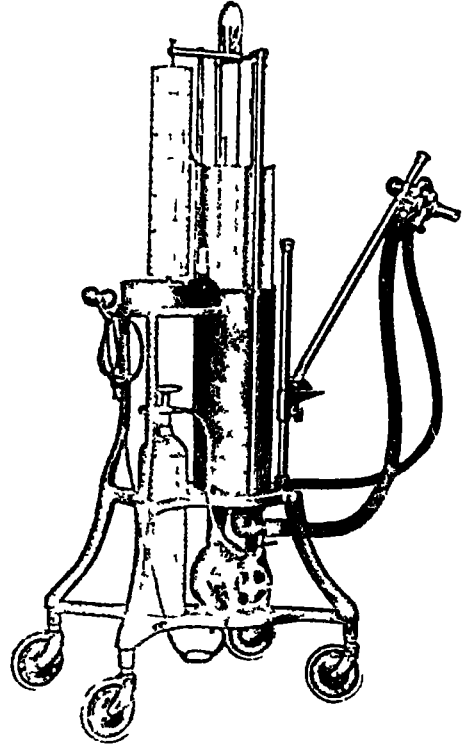
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## Address\*

By DR. GEORGE E. VINCENT  
*President of the Rockefeller Foundation, New York*

MR. Toastmaster, Ladies and Gentlemen: I have been in town all day but this is the first session of this gathering which I have attended. I offer no apology, but I do vouchsafe an explanation. I have had so much to do as a layman with medical meetings that I have stopped going to them entirely. I have so little immunity against suggestion of symptoms that I will not expose myself to this sort of thing any longer.

The last medical meeting I attended was a meeting of the New York Academy of Medicine which was devoting two weeks to the study of old age. They called it gerontology but it was the same old thing. They asked me to make an address at this opening gathering. I prepared one of those affable urbane and slightly cheerful views of old age which I hoped to present with something like optimism. I did my best. I did not say too much about old age. I did not try to gloss the thing over unduly. I had to admit that old age had its disadvantages but I expressed in a timid, tentative, modest way the hope that society might find some slight use for people who

are over seventy years of age. Then I made a great mistake. Having made my address, I didn't go away, I stayed and I listened to one of the most diabolically accurate and scientific pathologists that this world has ever produced. He spoke for an hour and a quarter. He spoke about old age with a definiteness, with a cold-bloodedness that was absolutely unendurable, worse than that, he displayed before the whole company what might be called a time-table of senility. All the symptoms were shown appearing at a certain age. I had every one of them coming at precisely the scheduled time. Then he went on giving detailed, pathological, imaginative, descriptions of old age, and his general conclusion was that he couldn't for the life of him see why anybody with common sense and who wasn't already the victim of softening of the brain should want to be a victim of old age. He thought some people might possibly go on to seventy, but why anybody wanted to go on longer than that he could not himself imagine.

I haven't gotten over that yet. It was a gloomy and depressing evening, and, therefore, I resolved that I would subject myself to nothing of that kind tonight. I looked over your program and it was full of the most damaging

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\*Delivered at the Annual Banquet of the American College of Physicians, April 11, 1929, Boston, Mass.

and dangerous possibilities I am glad to say that I haven't heard a single word that any of you had to contribute on any of these subjects, and I do not propose to read any of the papers if they are published (Laughter)

I have been introduced as a doctor, but I want it distinctly understood that I do not vent myself as a doctor. A long time ago I got the degree of Doctor of Philosophy. I did not parade it. I wouldn't go so far as to say that I am ashamed of it, but at the same time when I associate with doctors of medicine, I realize the patronizing superiority with which they look down upon me and I am increasingly willing to be called "Mister," or even "George E. Vincent" (Laughter). But I got that degree of Doctor of Philosophy a long time ago, because then I was by way of being what was called a sociologist. I no longer acknowledge being a sociologist, but I still have a certain hankering after sociology. I have a sort of wistful, backward look at my sociological days, and when I see gathered before me a co-educational company of this kind, it brings back the old days of my professorship. It seems as though this were one magnified classroom and I find that my—and that is one of the signs of senility which appeared on the chart to which I have just referred—inhibitions are weakened and that old habits reassert themselves and that gerontism of a certain kind takes possession and will have its way. Therefore, I propose this evening, in order to put myself in some degree on an equality with you, although I have listened to none of your technical ad-

dressess, to make a sociological address. You might as well know it at the outset. If you have come to the city of Boston with the idea that you are going to enjoy yourselves in any purely frivolous way and not make appropriate sacrifices to what is sometimes courteously called the intellectual life, you are greatly mistaken. You have either got to exert your higher hemispheres or, what you have so frequently done, give the external signs of that kind of inner activity.

I want to present to you a sociological theory, though I realize that it has certain disadvantages. My children urged me never to use slang. They say it dates you so. So my sociological theories date me dreadfully. I have no doubt these sociological theories have long since been abandoned. I am sensible enough not to refer to Herbert Spencer. I know that no one thinks of him except as a delightful archeological specimen of a perfectly desiccated form of thought which no longer plays any part in the world except possibly south of the Mason and Dixon Line where it still serves the purpose of holding up a dreadful example of what atheism combined with intellectual achievements may do in the way of destroying human character and menacing the very existence of society (Laughter). But I do revert to a theory which you will see a little later on is not wholly unrelated to the interests represented here tonight, to the theory of a French sociologist, Gabriel Tarde. In the days to which I refer, people were always trying to find some criterion of the essence of sociology. You got on very well with physics and chemistry. Then you

came to biology, and in trying to explain the differential you used "vital." Of course it begged the question, but it was useful, and, therefore, in biology you deal with vital phenomenon and later on philosophically discuss what you mean by vital, but at any rate it is something. When you go on from the biological into the psychological field you bring in consciousness although I believe Watson has ruled out consciousness. You see how far behind the times I am. Then when you come to the sociological you also have to have some sort of differentiation. What is the differentiation? Well, there was Professor Giddings who said it was consciousness of kind, and there were other people who said it was contact. That was before the advertising men made the term a household word.

There were others who thought it was a contractual relationship, but Gabriel Tarde said the essence of social relationship is imitation. He developed a most beautiful theory which he expressed in graphic terms with a picturesqueness which took the imagination. "Society," said Gabriel Tarde, "is like a vast plain and rising in this vast plain are certain mountains, and on the summit of these mountains are gorgeous individuals and groups, held up into the sunlight so that they can be seen of all the people in the plain."

These heights are the models from which imitation is spread through the masses down into the plains. Every society has its glorified heroes, every society has its élites, and it is these heroes and élites that to a very large extent determine the very nature of society and control its activities,—a

very interesting theory when you come to think about it. You have no social organization unless there are, raised above the levels of the great masses of the people, these glorious mountain peaks for imitation. These are the models, says Tarde, and by imitation these models spread from individual to individual until they influence all the group, and of course with present day communication (Tarde's theory was propounded before we had the radio), the rapidity with which these marvels are spread from sea to sea and from continent to continent is simply the amazing phenomenon of our times. But it is a very interesting theory, this theory that after all a large part of society itself is constituted of centers which are imitated and that the great essential social process is the process by which necessary mountains are raised and the process by which imitation flows from them to the control, influence and management of great masses of people.

Let us examine it for a moment. What do we mean? Of course every society makes its heroes. These heroes are shining examples. These heroes have the greatest influence. These heroes are held up, they are concrete examples of the things which the group prizes, the things which the group admires, the things which the group imitates. Of course society makes its heroes, so to speak, to order. Under given conditions it has one kind of heroes, change the conditions and another sort of heroes are immediately demanded. Some of you can remember the Spanish American War—some of the men. (Laughter) The Spanish American War, of course, compared

with recent conflicts was rather a pitiful affair, but as the Irishman said, it is better than no war at all, and it is a war with respect to which we came out very handsomely. To be sure, most of our sacrifices were due to typhoid fever and other communicable diseases in our camps, but we got a few men to the front, and they were comparatively safe when we got them there. But we had heroes. We created military and naval heroes. Of course they were rather perishable, they are a perishable lot. We gave an allowance to one and kissed another, and they rapidly disappeared. (Laughter) For the time being they were exalted, they were, as Tarde would say, on the mountain peaks, and you can imagine how we were influenced, how we adults were influenced, how our boys and girls were influenced by these glorious if transitory instances of models of heroic conduct and personality set up before us.

I think if we will go on to examine things a little more carefully we will discover that after all the heroes are in an exalted manner typical of groups and that in reality the one enduring social force is not the individual but the small group of which that individual is an outstanding and conspicuous example.

Lindbergh, of course, is a great hero. Thank God up to the present time he hasn't recommended a thing for the purchase of the American people, and that, now, is the sign of true greatness. He represents in a supreme way that exalted group who represent averages. It is the group after all from which the hero gets his

meaning. It is the group into which the hero sooner or later is merged, it is the hero who temporarily gives distinction and prestige to his group.

Therefore, the thesis that I want to propound a little while tonight is that it is the élite that determines to a very large extent the progress, the course of modern society. The élite, the small selected group, has immense influence in social organization, immense influence in social conduct, immense influence in that thing which we are not perfectly certain is true, but which for preambulatory purposes we describe as the progress of society.

The élite is a very interesting idea. Of course it is unpopular in a democracy, and what I want to talk about tonight is the élite in a democracy. The élite in a democracy is resented. The very idea of the élite seems to be contrary to the underlying conception of democracy, which is that everybody is just as good as everybody else. That, of course, is an entire misconception of democracy, but most of our conceptions about ourselves are entire misconceptions, and, therefore, we have contrasted frankly, and let us admit it at the outset, the idea of the élite with the idea of the many. The few competent are always an insult to the incompetent many, and the incompetent many at the same time that they grudgingly admire and follow the élite, when the fact that it is the élite is pointed out to them, are universally resentful.

It is one of the most interesting things to observe that we despise and abuse and attack the things that are essential and that we sneakily admire. This applies to the élite known

as society. Of course it is a little difficult now to be quite sure just where this is. In the good old days that I can remember, we had a 400 in New York and it was a great comfort to have a 400. You knew then when you were in, and most generally when you were out. There was something distinctive, there was something satisfactory, there was something definite, and when Mrs. Vanderbilt was in charge it was very definitely known who could get in and who couldn't get in. Those were the good old days of the 400 and Ward McAllister and Mrs. Vanderbilt and the great balls that settled who was who and who wasn't.

That was a very definite sort of thing, but now all things have changed. You can't be perfectly certain, and yet in a way if you are on the inside, you know a great deal more than you do if you are on the outside.

In a very definite way there is a society. There is an inner circle, then another circle, then another circle, and then still another. And the people who are in the very inner circle know very well where that leaves off and the other one begins. It is only the people outside altogether who think it is very easy to get in. Moreover, there is always the resentment. Whenever you hear a woman say that she wouldn't go if she could, if you know anything about psychology, you know then that the group exists, and exists very definitely. (Laughter)

Democracy resents the very idea of this exclusiveness, for exclusiveness is one of the characteristics of the élite. The definition of the élite is the selec-

tion of the few from the many, and you can't select the few from the many without leaving most of the many outside. That is precisely what happens. It happens in all sorts of ways. It happens in social clubs. There are clubs continually being formed. They are usually organized by the people who can't get into the other clubs and it is a very good procedure. If you can't get into an existing élite, start one of your own, and after a while there will be people who actually feel excluded from yours, and then you know that you have begun to get an élite. It is a process that in a democracy can go on, it has its disadvantages because there is a limit to the amount of glory that can be shed upon the rapidly multiplying élites. The game is all spoiled because there are a few of the older élites that still go on behind that kind of élite, and you can't quite imitate them. Your own élite is not quite as good, it is not exactly a substitute, but it is the best you can get under the circumstances.

I remember very distinctly that this sense of being excluded is one of the very interesting characteristics of the idea of élite. I was ranging once, when I was an undergraduate, through a library. To say frankly I got in by mistake. I thought it was a popular library where novels were circulated, and instead of that, I got into the university library. I was so interested to see what it was like, now that I was there, that I looked about and I was allowed to wander. I don't know how I got in, but they let me wander about, I found books of various kinds and I got interested in them.



It is a habit I went afterwards, but I was regarded as eccentric by my classmates, and I concealed the fact that I knew very much about the library. I did find a lot of very amusing and entertaining books. One of them was a little bit of a volume published in 1842. I took that out and found that it was written by an eccentric American who had traveled about the world a great deal. He was a graduate of Yale. He had all his honors on the front page, on the little title page, and here in the middle of this title page was this "Blackballed at the London Athenaeum Club, 1839" (Laughter). For a while I pondered, I didn't quite know what the Athenaeum Club was, but don't you see the idea? The very fact that he had been considered for the Athenaeum Club was in itself a distinction. I don't suppose in his time there was another American that had even been put up at the London Athenaeum, and he naturally strutted about because he had at least been considered.

This matter of exclusiveness is a very interesting thing. There is a Harvard man I know who says of the Yale Club in New York, which is on Vanderbilt Avenue and 44th Street, "Membership in the Yale Club confers all the unique distinction of being a member of the Grand Central Terminal." That wasn't quite kind, because it approaches in a way to accuracy. That is a club which could not be described as intolerantly exclusive. It needs the money for one thing, and it is a Yale Club for another, and Yale represents, as you probably know, even under the shadow of Cambridge, an American democracy

which is one of the most valuable, et cetera, et cetera (Laughter)

What is the essential characteristic of an élite that is a real élite? It has prestige. Prestige is the important thing if it is going to be a real élite and if it is going to function as an élite. It is a rather curious, entertaining, and a little disconcerting thing to examine the etymology of prestige. It has the same root as that of *prestidigitator*, and it means illusion, deceit, trickery, wonder, amazement, fascination. Therefore, prestige of the individual is an illusion about one's own importance which gradually is translated into a reputation. You see other people taking that illusion as a reality, until finally prestige has become identical with reputation, and better than that, with a glorious reputation which confers honor and distinction.

Isn't it amusing what happens to language when you let it go? So the prestige of an élite is that the bunkum of the past has become the illustrious, characteristic, outstanding and shining distinction of the present. But we need not quibble with the word, we know what prestige means. Prestige means that belonging to the group confers upon the individual who is a member of it a certain reputation, a certain standing, a certain distinction. What is distinction? Just something that that labels you a little and gets you out of the great common herd and mass of mankind. Everybody wants to be a little distinguished. There is nothing so bad as to be told that you are a completely average person. You are perfectly willing to admit that you are average because you want people to deny it, but you

dislike being told that you are average people. You know you are not. The whole object of your organization would be defeated if you were. You are not average people. You are extraordinary people. You are unusual people. You admit it. You take pride in it. You are doing your best to make other people envious of you, and you are gradually gaining prestige, which is what you are after. (Laughter) That is, you hope that in time the public will take you at your own valuation.

So our élites are characterized by prestige. Where do they get prestige? How can you go about acquiring prestige? It is rather interesting to analyze that a little. There is nothing better than antiquity. It seems irrational; it seems unfortunate, but if your élite is old enough, if it stretches back over generations, better if it stretches back over centuries, it becomes sacrosanct by the mere passage of time. It is one of the most irritating, one of the most annoying, one of the most utterly unendurable things that it is a real prestige and there is no getting away from it. One of the most delightful things is to suppose that by denying things, you can change the facts. You can't. The scientifically-minded person simply examines them. He may not like them, but he tries to face things as they are, and one of the most important forms of prestige is historic tradition. We laugh about the first families of Virginia. Why? Because we don't belong to them.

We make flippant allusions to Beacon Street and old Boston families, and how glad we would be if we could

claim even the most distant cousinly relations to them. They have real distinction, they have real prestige, and it is a prestige that has come down through the years and it exists, it may be irrational, it may be utterly without foundation, we may be in our splendid characters, in our marvelous intellects, in all the noble qualities which we possess in such copious degree, we may be the superiors of all these people, but the public doesn't know it. That is the important thing. Prestige is something that exists in the minds of other people, and if it is there, it's there, and nothing you can say about it will change it, it's there.

So there is a prestige of antiquity. Wouldn't you like to be a member of the Royal Society of Great Britain which was founded in 1660, and which has had associated with it a list of most brilliant names in the sciences ever since that time? To be a member of the Royal Society confers real prestige, historic prestige, and it is something that people covet and prize as a possession, and it is something which has the admiration not only of the British public but of people who know what reputation in science is the world over. It is an actuality, it is there, it exists and it will go on existing for generation after generation. It is very difficult to take what might be called sudden retrospective measures with regard to your family, for example. That is something that just can't be done. Therefore, the historic business takes care of itself. There is no way in which you can make your society older than it is. It was founded, I believe, in 1915, and there you are. It will take another hundred years to

make it sacrosanct, but the time will come, if you stick to it. It ought to be a joyous thing to you to think that your successors, whatever may be your humble position, will be on the mountain peak, bathed in the light of a prestige which has back of it all the sanction of antiquity.

Then there are what are called founts of honor. Royal approval and recognition are still, in spite of all the things we say about kings and queens and royalty, a sort of prestige. How many Americans take their daughters to the Court of St James and how many would like to? Of course, I wouldn't have that sort of thing, I don't prize that kind of thing at all, you know, "I wouldn't have my daughter go, it would interrupt her education, for one thing, because she doesn't get through school and college work until the end of June, and this comes in May. No, I don't see why mothers want that sort of thing." Ha! ha! (Laughter)

Thank goodness I have never said that. I have two daughters but they didn't get to the Court of St James, and I would be a hypocrite if I said I might not have taken a certain satisfaction if they had. Let's be honest about these things.

There is real prestige still in recognition by royalty. Look at the birthday honors. Oh, of course we know the king doesn't do it himself, no, but he is the source of prestige, he is the immediate source of prestige. Oh, yes, yes, they contribute to the campaign funds those knights and baronets and all the like, yes of course. Well, perhaps they do, who knows. At any rate it carries distinction. When you

meet an Englishman, are introduced to him and he is introduced by a title, of course your democratic spirit is revolted, you don't think a thing more of him because he has got a title. Don't you? Of course you do, you know you do. That is the truth. These are the facts. What is it that goes on in your mind? What do you really think? Not analytically, not reflectively, not on a high moral plane, but how do you sneakily feel about it? That is the real thing.

Then there are institutional sources of honor. For example, our universities. Our universities give degrees, they give two kinds of degrees, degrees for work done, and degrees as an honor. They are founts of honor for us. Look at the lists of people who have degrees at commencement time. Of course sometimes it is a little embarrassing; sometimes it is a little funny. I can't help having respect for two or three rich men I know who give money to colleges and universities but who absolutely and always refuse to accept an honorary degree. Some might call it humor, some might call it modesty, some might call it good taste, it is just as you feel.

Our universities are sources of honor, they are founts of honor, they put hallmarks on people. All the members of your college have a university hallmark of some kind. You couldn't get in if you didn't have it. Self-made people need not apply. You have got to go through and be stamped by somebody. Of course oftentimes under our democratic conditions you have to explain pretty carefully who stamped you, because there are élites among universities. That is what some

of our English friends who get honorary degrees for a price don't understand. The National University at Washington, for example, which confers degrees of all kinds by mail at twenty-five dollars up or down, does not confer in the United States an enormous amount of genuine prestige but in some foreign countries where they don't go into these things, or haven't until recently, no questions being asked, the degree coming from an American institution has conferred a certain amount of very modest distinction.

We have other sources of honor. We have academies. You know we have a national academy, an Academy of Sciences in Washington and it is a distinction to belong to that. I don't suppose you know as much about that as you might, but if you did know about it, it would be something of a distinction. (Laughter)

We have, of course, the classical example of the French Academy—the forty immortals. Well, we have an academy that was started by Mr. Howells and a group of people, and a very fine group it is. The only trouble is it hasn't been going on long enough. A couple of hundred years from now it will have a great deal of prestige, undoubtedly, throughout the United States. Now it is in the process of growing its prestige and if you examine it carefully and see what good men have belonged to it, you will feel that they have made an excellent start, but at the same time we have to admit that it does not have anything like the prestige of the French Academy—the forty immortals.

Then there is the prestige of prizes. The Nobel prize confers a distinction. We don't quite know who the Nobel people are, who award the prize, but we assume that they are very capable people, and when they give the prize, at once the individual who gets it enjoys prestige and distinction.

These are illustrations. I need not bore you with more. There is institutional prestige. Then there is a kind of prestige which seems to come from a sort of public admiration such as applies in a very humble and amusing way to some of our screen stars. Of course some of them are going to suffer. I think very much because a few just have looks and not voices and under the changing conditions, voices are going to count quite as much as looks, so that a combination of appearance with voice is now going to make a new selection and we will have a new élite from Hollywood.

There is a kind of pathetic élite made by the great masses of the American people who hold these heroes and heroines up until they become set apart as tinsel Olympians, who after all have a kind of prestige. They exercise an influence, they are admired, I suppose, by millions of people all over the United States in a form of spontaneous, democratic apotheosis.

When we come to examine the essence of élites, we will discover that a limitation of numbers is a very useful thing. We are going to have just so many people and when we come to that limit there is going to be a waiting list. A waiting list always adds to a club's prestige. Sometimes they make the waiting list just on purpose to confer the prestige. A waiting

list is an enormous suggestion of a cue waiting to get in and kept waiting to get in. There is a certain satisfaction on the part of those who are inside to have those on the outside wait until there is a vacancy. Of course it is very fortunate for the people outside and they take a morbid interest in mortality tables as applied to those who are on the inside, but the limitation of numbers is a very important thing and you will find, I think, that certain élites which enjoy the greatest distinction are those which have a limitation of numbers.

If the idea is to raise the group to the very highest pinnacle of glory and to hold it there in the very sunlight of the utmost possible prestige, the forty immortals is a classic example. If there were a hundred immortals, they wouldn't be nearly so immortal. It is the limited number, and then every time an immortal dies, that canvassing of candidates, this man and that man, will he be chosen or will the other? It is a tremendous play of popular attention upon the prestige of the group, upon this conspicuous élite.

But there are élites that seek another thing. They seek a certain standard, a certain type, a certain ideal. They say, "We will not limit numbers but we will hold true to that standard," and let there be as many people as possible who can measure up to that standard, "so long as we hold to the standard we are not interested in limitation to any particular number." If the standard is high enough, you really have a limitation of number, because anybody who is at all familiar with statistics as applied to biology, as applied to psychological characteristics of

individuals, knows that in any group there is a very small percentage of people who can be regarded as exceptional, as belonging to a high pinnacle of distinction—sometimes five per cent, and that is a pretty high percentage.

Now we will come down to your college. The application isn't going to be nearly as long as the preliminary. If I understand properly, your college is not an élite which sets a limit. There is an organization I believe that has assumed that 150 physicians would be the limit that it could reasonably expect to find in the United States. I don't know just what the standard is, it must be fairly high. There you have a limit, and I have no doubt there are people here (they would deny it very likely) who secretly cherish the ambition that when the mortality tables have done their duty there will be vacancies in that group which humble but competent people are ready to fill. Far be it from any member of this organization to be derelict in duty, he is prepared to go to the front and take his place when summoned. That is the right spirit. (Laughter)

Let us now examine very briefly the problem which you are facing. You are facing the problem, as I understand it, of setting a standard. Why are you setting the standard? What is your object? Of course your object is the public benefit. That, we take for granted. There is no selfish motive to animate you for a moment. In order that the standard may be raised for the welfare of the American people you are ready to sacrifice your friends, relatives, and other people who may have social ambitions in

the interest of the public, you are adamant. This is a noble position and I applaud it highly. You are bound to stand by and see that this standard is preserved.

What are the difficulties? The difficulties, of course, occur to you, you have thought them over better than I have, but I am talking from an outside point of view, sympathetic, interested, wishing you well.

Let me consider first of all with an *a priori*. I know nothing about your experiences, but as a reformed and retired sociologist I am *a priori* aware of certain speculations about human nature. There are certain internal difficulties. I have belonged to a few clubs, under very embarrassing situations, because we raised the standard after we got in, and when we had to break it to other people that they did not measure up to the standard, they raised a row. They said, "How did you get in?" All we could say was that we were on a new basis. (Laughter)

You are bound to have differences of judgment and there are always people who will feel that they have been unfairly excluded.

Then there is always the temptation, and it is a very real temptation, a kind of pleasure, of saying, "He is an awfully good fellow. Yes, of course he hasn't done very much lately and he has rather run on momentum since he was graduated, but he is a splendid fellow. At that St. Louis meeting you know he was the life of the party." (Laughter) I may say, by the way, if you are hard-put to it for festivity, I hope it won't go any further but I

could suggest Hoboken, New Jersey, as a place. (Laughter)

Then of course sometimes there are people who say, "We think this thing has gone too far and we don't want to be disagreeable, but if you are not a little more lenient we will see, we have had quite a number of members feel that things are going a little far and we will see what can be done at the next meeting in the way of getting some other representatives on the selection committee," and so on. There are always those internal possibilities. There is no doubt about it, there is pressure brought to bear and it is a temptation to be a good fellow. There are people who go so far as to say that democracy is incapable of making its own élites from the inside, that the very essence of democracy is such a sloppy sort of good-natured comradeship that it is impossible to get a group up and hold it there, that it gets pulled down toward the great level of mediocrity which is such an enormous majority.

There are about 120,000 doctors in the United States, not counting some of those irregular people who give you such anxiety. About 80,000 of them belong to the American Medical Association. There is only one society that I know that is more exclusive, and that is the National Geographical Society. (Laughter) The American Medical Association, then, is the starting point. You begin to cull from the 80,000, you rule persons out on various grounds, and then you get to your organization with about 2,000. That looks to me as though you were pretty nearly approaching a limit. I don't know what your plans are, but

unless these doctors, unless the 80,000 doctors are a very extraordinary lot—and I am not sure that they are—you are getting pretty close to a safe élite out of 80,000. You might go another 500, who knows, and of course in time you will lift them to your own level.

A great deal has been accomplished. American Medical Association has done splendid service in raising the level of medical education in weeding out old and weak schools. Let us admit it. More than that, let us be grateful to the American Medical Association for what it has done in raising the general level, and you never can do very well with an élite until you have got a pretty good level to start from. When you are in Denver, Pike's Peak is very high because you start a mile high to climb it, and when you are starting an élite, it makes a lot of difference whether you are selecting from a very good level that has been attained and then are getting élite from that or whether your élite is made from very common, ordinary material.

The American Medical Association has contributed enormously to raising the level from which you are to make selection.

Now we will turn to the external form of the thing. Of course you have been broadcasted now so there are probably a lot of people in Brookline and other suburbs who have heard about your organization. It goes slowly. Of course you can try putting the initials on your cards, but I would go a little slowly on it because, you see, they might think you were a chiropractor. (Laughter) You can't be

too cautious about these things. I remember very well a Methodist minister here in Boston, oh, a great many years ago, a young fellow. My father was a bishop, and I used to go around with him, and we visited some of these preachers. This preacher was very proud of his education. He was utterly without humor, he took himself very seriously, and he printed his degrees on his card—Rev James B Jackson, B D A M. An old presiding elder came around. He was one of the old kind that hadn't been to college, but was a pretty hard-headed old boy with a real sense of humor. He looked at this card and said, "Jackson, you ought to get one of these colored colleges down South to give you the degree of Doctor of Divinity, then your card would read—"Rev James B Jackson, B.D.A.M D D" (Laughter)

You have to be very careful about degrees until the public has been educated.

The great difficulty about an élite is that it isn't an élite until a lot of people know that it is, because you see it exists really in the minds of other people. You may not know it, but if the public doesn't know it, what satisfaction can you get out of it? President Hadley said a thing years ago that has never been fully understood. He said, "You can never be sure that a law is really understood until the violation of it causes a man to be socially ostracized. When a man is put out of his club, then you will know that society is expressing a judgment." But you can refuse to answer questions.

Your cronies will go around and slap you on the back and say, "Go

ahead "The Senate be damned" That man doesn't care much what the great mass of the public think as long as his cronies stand around him and tell him to show disrespect for the elected representatives of the American people It is what your cronies think and what the people whose opinion you care for means to you that after all counts, and so an élite that is going to be a real élite must be an élite than stands high in the opinion of the people that will be affected by the creation of the élite That is going to take time I hope the time will come when membership in your college will be a thing that people will know and understand I know about it, and after you have gone a little while, when something happens to me next, I am going to ask my doctor why he doesn't belong to this society, because I am going to reach the point where I will refuse to have anybody look after me that doesn't belong to the society (Applause) Isn't that the test? Isn't that what you are working for?

If I were taken down with what seemed like appendicitis in London, I would feel very much better if I were going to be operated upon by somebody who belonged to the Royal College of Surgeons, because I would know that he had been through one of the most rigid, absolutely impersonal and detached examinations as to his ability and that he had gotten through after this most careful scrutiny and therefore those letters after his name would mean so much to me that I would feel added satisfaction and confidence if I knew that he had been certified to in that way

That is what we need in this coun-

try Do you realize—of course you do. I needn't talk about it, but one of the great needs in America is an ability on the part of the public to discriminate in the choice of doctors and surgeons That is the real test of intelligence, and little by little an organization like yours is going to help intelligent people to make selection

You are not moved by any commercial ideas, you are not thinking at all of making yourselves more available and more desirable, your one aim has been and is to educate yourself and to raise yourself to higher levels to efficiency, and in due time a reasonably increasing intelligent public will realize you have achieved this and will feel more confidence in you

In reality, what you are seeking in your organization is one of the most important and vital things for the American people You are attempting to set ideals and standards You are attempting to bring into comradeship—for after all that is what a college means, it means a group of colleagues with common aims and common purposes—a group of people who have had training, who are going on in self-education and in mutual education, who are growing day by day, who are attempting to keep pace with the rapid increase of knowledge and of skill which are made available for the public You are trying laudably to create an élite, an élite based not upon tradition, an élite based not upon factitious or adventitious glory, but an élite based upon achievement, upon gradual, steady growth in knowledge and in power and in loyalty and in comradeship



I offer you my heartiest congratulations. You have no illusions as to what you have set out to do. You do your work today and tomorrow and trust to others who come after you to take up the tradition and carry it on. I have little patience with a man who can't do anything until he sees the dawn of the millennium. My loyalty and admiration are for the men who do each day's work with a goal a

little ahead, resolved to do as best they can, and to pass on an improved tradition to those who come after them.

May the College of American Physicians gain steadily, slowly but steadily, the position of a true élite in a democracy, an élite which claims prestige solely for honest achievement, for loyalty to science, for devotion to the welfare of the profession and to the service of the public. (Applause)

# Serums and Vaccines in the Prevention and Treatment of Disease\*†

By BENJAMIN WHITE, Ph D, *Boston*

THE present popularity of serums and vaccines rests upon the known efficacy of such time-proven products as smallpox vaccine and diphtheria antitoxin, partly upon the hope that some of the newer and less thoroughly tried products may ward off or modify a disease, or sometimes upon the very human wish that even if we are sceptical, we can at least be doing something for the patient

As biologic therapy progresses it is fitting, and it may be useful, to make as careful and critical an appraisal as possible of the many serums and vaccines that are now offered to the medical profession. For such an appraisal we have several criteria upon which to base our judgment. There is first our knowledge of the chemical constitution and the physiological action of these agents and of the immunizing response they call forth when injected into the animal body, and then there is the clinical experience which has accumulated with their use. From the standpoint of theory we can predict with a considerable degree of accuracy

the general effects which may follow the injection into the body of foreign proteins such as those in bacterial vaccines and in horse or other animal serum products, although we may not have a complete explanation of their actual mode of action. Furthermore, we have acquired a great deal of reliable information about the nature and extent of the protective or immune mechanism that functions as a result of the parenteral introduction of viruses or inanimate protein matter. To be sure, there remains much unexplained detail in these immunological processes and many phenomena which have not yielded to our present methods of study, yet we possess sufficient sound knowledge to say what one might or might not expect from the immunizing action of this or that serum or vaccine. When we draw upon clinical experience for our estimates, however, we must limit ourselves to mass or prolonged experiences or to carefully studied parallel series of cases treated with serum or vaccine and similar cases in which there was no such treatment.

Speaking in a general way we may safely say that one might expect vaccines or similar antigens to produce more or less active immunity and, therefore, some specific resistance

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†From the Antitoxin and Vaccine Laboratory of the Massachusetts Department of Public Health

against the particular disease represented by the vaccine or antigen, and that in acute disease they would have little curative effect beyond whatever possible beneficial physiological action may come from their alien protein nature. With serums one could reasonably say that a potent serum would protect against related infection from a recent exposure or, for a short while, from imminent exposure, or would confer upon the recipient temporary specific resistance against an already existing infection. The possible action of serums and vaccines in diseases due to causes other than infective agents is still on such a speculative basis that any consideration of this kind of therapy may be omitted here.

With these general principles in mind, the various vaccines and serums usually employed in the prevention and treatment of infectious diseases may be discussed as follows.

A preliminary definition of terms may serve to excuse certain seeming inconsistencies. Under "vaccines" are included preparations containing viruses, either living, attenuated or dead, the products of bacterial metabolism such as toxins and so forth, and proteins of non-microbic origin, as those from pollens and food-stuffs. For the present purposes this term applies to these agents whether they be used to determine susceptibility or resistance to infection (Schick toxin, Dick toxin, and some tuberculins); to produce active immunity to anticipated infection (vaccine virus, typhoid vaccine, Dick toxin and diphtheria toxin-antitoxin mixtures); or to exert a curative action where infection has already taken place or infectious disease exists

(rabies vaccine and some bacterial vaccines). "Serums" might embrace the blood serum of normal animals, the serum or refined serum globulins of animals immunized against toxins (antitoxic serums, such as diphtheria or tetanus antitoxins), or of animals immunized by the injection of bacteria or their products other than toxins (antibacterial serums, as antimeningococcic serum and pneumococcus antibody solutions amongst others). Such use of these two names, loose as it is, can be said to be far more accurate than their usual employment.

## I VACCINES

The efficacy of a given bacterial vaccine for prophylaxis may be forecasted with some assurance. If the organism used belongs to a homogeneous group, such as Type I pneumococcus or typhoid bacilli, if it is capable of producing readily a definite stimulation of antibodies, if the titre of antibodies so produced is maintained at a reasonably high level over a worth-while period, if the disease is a manifestation of bacterial invasion as distinguished from toxemia, and if the vaccine is not of itself so toxic as to preclude its use, then we may expect that a suitably prepared vaccine of this organism will be of value. A low rating in any one of these particulars, on the other hand, may be sufficient to render the vaccine useless as a prophylactic. When these vaccines are used for their specific or non-specific therapeutic effect, considerations similar to those just mentioned apply to such use.

I *Acne* The acne bacillus has been shown by experiment to have a low antigenic coefficient, and one

therefore would not count on it in vaccine form to produce marked effect upon any infectious process caused by it. Vaccines made of suspensions of this bacillus, either alone or combined with the usual skin cocci, have been employed in the treatment of this obstinate condition. It has been recommended that they be used in fairly large doses in conjunction with appropriate treatment of the skin and with general hygienic and dietetic measures. Even then their curative effect is not particularly notable. Persistent vaccine treatment, however, may benefit cases that have not yielded to other treatment, and in those patients where no improvement follows it is possible that there may be biologic differences between the strain or strains injected and those infecting.

2 *Allergy to Food and Pollen Proteins* Hypersensitiveness to foods, plants, dust, dander and a host of varied substances presents a wide field for exploration. Already we have a bewildering list of preparations—the so-called “allergins”—for diagnosing and treating these various states of hypersensitiveness. Their number, and the complexity of the problem may excuse the omission of their discussion at this time.

3 *Antivirus (Besredka)* Besredka has proposed the use of sterile filtrates of broth cultures of staphylococci, streptococci, colon bacilli, gonococci and other organisms for local application or irrigation in infections due to these various bacteria. His theory is that the growth of such microorganisms produces in the broth substances specifically antagonistic to the species, and that these substances when applied

to the infected tissue inhibit the growth of the causative organism. These products are manufactured by many of the European laboratories, but both laboratory experiment and clinical trials by competent observers in this country have, in the main, given disappointing results.

4 *Catarrh, Common Colds and Influenza* For both acute and chronic infections of the upper respiratory tract a number of vaccines are offered, containing a few or many of the following bacterial species, influenza bacilli, streptococci—both hemolyticus and viridans—, the three types of pneumococci, Friedlander bacilli, Micrococcus catarrhalis and staphylococci (aureus and albus). There is little scientific basis for using such polygenic mixtures to prevent infections of such uncertain etiology. Their use, of course, is directed against secondary invaders, but even then we should expect that the Pfeiffer or influenza bacillus, Micrococcus catarrhalis and the streptococci would produce little or no immunizing effect, although pneumococci might establish a slight, transient immunity. These vaccines are widely used, and many clinicians claim that where no anatomical abnormality or pathologic lesions are present their vaccinated patients usually escape the common respiratory infections. During the 1918-1919 pandemic of influenza and subsequently, studies have been made on several large groups to determine the immunizing value of influenza and allied vaccines. In these groups, approximately one-half of the number of subjects were vaccinated and the other half not vaccinated. McCoy, after analyzing the incidence of

acute respiratory disease in some of these groups failed to find any evidence that the vaccinated persons fared any better than the unvaccinated

5 *Asiatic Cholera* Bacterial vaccines made from the cholera vibrio are antigenically potent in producing a fairly high degree of resistance to this disease. This immunity is neither absolute nor enduring, yet when kept at a proper level by semi-yearly or yearly vaccination it suffices to give excellent protection to troops and travellers, to physicians and nurses, and to members of communities where the disease is endemic. Some of our commercial laboratories offer this product with conservative claims in regard to the duration of the immunity produced.

A novel and apparently reliable means for preventing Asiatic cholera is the use of the bacteriophage as proposed by d'Herelle. This agent obtained from sewage or from cultures of cholera vibrios and other organisms has the ability to dissolve these vibrios both within and outside the body. When the proper "phage" is added to polluted water supplies it reduces the number of virulent cholera organisms to such a low point that the water is practically incapable of causing infection and, when given to man by mouth, this same phage will dissolve many of the vibrios ingested and prevent their multiplication in the intestine. The results of d'Herelle's work in India will be watched with the greatest interest, because if successful his method provides a simple and cheap way of rendering polluted water safe and also of protecting the individual.

6 *Colon Bacillus Infections* Because *Bacillus coli* and other bacilli of

the Paracolon group are found in many infections in or about the gastrointestinal and urogenital tracts, vaccines made from these organisms are used in their treatment, and sometimes before surgical operations to prevent infection. Bacilli of this type have the peculiarity of inducing an immunity specific for the one strain injected and it seems unlikely that whatever immunity might follow the injection of a stock vaccine would cover the many strains encountered in these varied conditions. One's chances of success, therefore, would appear greater with the use of autogenous vaccines, but even here it may be questionable if any improvement in the patient's condition may not be due to some accompanying form of treatment.

7 *Combined Vaccines* Any vaccine composed of *B. coli*, *Pneumococcus* I, II and III, *Streptococcus* (hemolyticus and viridans), *Staphylococcus albus*, *Staphylococcus aureus*, *Staphylococcus citreus*, recommended in cellulitis, phlegmon, septicemia, puerperal sepsis, abscesses and other septic conditions would seem to be a decidedly hit or miss form of treatment. Now that competent bacteriologic service can be so easily obtained, there seems no need for neglecting the diagnosis or for injecting such a bacterial mixture in the hope that it might fit the case.

8 *Diphtheria Toxin for the Schick Test* The skin reaction, or absence of it, to the intradermal injection of diphtheria toxin is an accurate index of susceptibility or resistance to diphtheria. If the results are to be reliable, however, only fresh Schick outfits, kept continuously cold should be used,

and the exact amount of diluted toxin specified in the directions accompanying each outfit should be carefully injected superficially into the skin. With close attention to these details the technical error should be two per cent or less. This test should *always* be made on persons receiving toxin-antitoxin injections six months after the last injection of this mixture. Other methods recommended for the routine determination of immunity to diphtheria in human beings possess no advantages over properly done Schick tests.

9 *Diphtheria Toxin - Antitoxin Mixture, Toxoid, Anatoxine* With such efficient means for producing active immunity to diphtheria it seems inexcusable to permit children to pass from infancy without this protection. The one-tenth L plus toxin-antitoxin mixture given subcutaneously in three doses one or more weeks apart will immunize the great majority of those so treated. The dose should be exactly that given in the directions. The ensuing immunity should always be checked by a Schick test performed six months after the last injection and should the test be positive a further course of toxin-antitoxin should be given and the person again retested.

There has been much discussion about the action of toxin-antitoxin mixtures in sensitizing to horse serum proteins. They undoubtedly do render some of the recipients allergic, but it is doubtful if the degree of hypersensitiveness so produced leads to harmful results when such a sensitive person has later to be given any other product of horse serum. An accelerated or aggravated attack of serum sickness

may occur in such an instance, but it hardly seems advisable to replace horse antitoxin in the toxin-antitoxin mixture with antitoxin made from the goat or sheep. As a matter of fact, toxin-goat-antitoxin mixtures have been found in some cases to cause more severe local reactions than does the usual product.

The ideal immunizing agent would be one containing diphtheria toxin robbed of its toxic but retaining its antigenic properties, and one giving few, slight or no reactions. This ideal is being approached with the development of the so-called "Toxoid" or "Anatoxine." These preparations in which the toxin is detoxified with formalin are harmless, have high immunizing value and give rise to no reactions in younger children. They do, however, cause local or general reactions in persons sensitive to diphtheria bacillus protein, and therefore, should not be administered to persons over five years of age unless the individual shows no pseudo element in the Schick test or a negative reaction to an intradermal injection of the toxoid or anatoxine. Persons reacting positively to either of these tests may be given either toxin-antitoxin mixture or toxoid in a longer series of divided doses.

10 *Gonococcus Vaccine* Such vaccines have been widely used in both acute and chronic gonorrhoea and its complications, but usually with disappointing results. Like other Gram-negative cocci, the gonococcus is capable of stimulating only a low grade immunity, and it is not to be expected that in a vaccine it would arrest the acute process or influence deep-seated

lesions In Europe, this vaccine is administered in the early stages with the belief that subsequent localization of the gonococcus will be prevented

11 *Pertussis* There is much debate about the value of vaccines made from the Bordet-Gengou bacillus, alone or mixed with various bacteria common to the upper respiratory tract, in the prevention of whooping cough Laboratory experiment has shown that B pertussis is a feeble immunizing agent, and, therefore, one would anticipate that its injection would, at best, give only a slight immunity, so slight, that infection would rarely be prevented, but perhaps sufficient to strengthen somewhat the body's natural resistance to the effects of the disease This anticipation is fulfilled in practice The value of the secondary organisms in the mixed vaccines is subject to the criticisms made under catarrhal vaccines Many physicians still hopefully administer this vaccine routinely to all children exposed to whooping cough, but the results, so far as protection goes, are not impressive Quoting from a previous article by the author, "Clinical reports as to the ability of vaccine treatment to prevent or mitigate an attack of this disease are not in agreement The majority of these reports are uncontrolled and, therefore, the worth of their evidence should be discounted The Danish reports are favorable as is also the report of the Harvard Whooping Cough Commission A critical analysis of the latter report, however, shows an absence of proper controls and that the results obtained with the vaccine were not clear cut or convincing. In other series of observations extending over a

period of several years where children were vaccinated with small and large doses of fresh and old vaccine and where alternate unvaccinated children were used as controls there was no appreciable difference in the whooping cough experience between the vaccinated and unvaccinated children

"While there are many enthusiastic users of pertussis vaccines, the whole evidence would seem to indicate that such vaccines, whether simple or combined, are of doubtful value, and rank low in the list of biologic agents"

12 *Plague* Although one attack of plague usually confers a life-long protection upon the survivor, vaccines made from *Bacillus pestis* confer only an incomplete and transient immunity McCoy and Chapin state that there is no evidence that such vaccination has ever controlled an epidemic However, because of the deadly nature of this disease the individual who may be exposed to it might seek such protection as these vaccines afford The best known of them is the Haffkine, although those prepared by other methods are probably equally as good It should be remembered that the plague bacillus is toxic for human beings and accordingly one may look forward to systemic reactions of some severity following the injection of this vaccine

13 *Pneumococcus Vaccines* Experiences with pneumococcus vaccines for the prevention of lobar pneumonia both in private and military practice have not been encouraging On the other hand, the work of Goodner and that of Barach, indicate that the injection of heat-killed pneumococci into the body sets up a definite immunity to the type of pneumococcus injected

This immunity lasts for only a short time (probably less than two months) but where the disease is uncommonly prevalent, or for persons particularly susceptible to it, the frequent injection of a vaccine containing the three main types may serve to avert an attack

#### 14 *Rabies Vaccines*

a) *Human* The increase of this disease in this country brings more and more inquiries as to the best vaccine to use and the preferred manner of administration. Rabies vaccine, whether it be the attenuated living virus made by the classic method of Pasteur, the diluted living virus of Högyes, the dialyzed preparation of Cumming, the dried virus of Harris or the phenolized virus of Semple, when used soon after the patient is bitten may be counted on to prevent the disease in nearly every case. When the wound is severe, when the bites are multiple or when they occur about the head and face, treatment should be begun at the earliest possible moment and the full course of twenty-one injections should always be given. In some of the European countries vaccinal treatment is given only at designated institutes where the patient is hospitalized and guarded against physical or emotional stress for the purpose of reducing the possibility of post-vaccinal myelitis or paralysis. Happily such sequelae are rare, but they do sometimes occur and precautions should be taken to guard against them. One of the conclusions reached at the last International Rabies Conference (1927) was that, "Such paralytic accidents are less frequent if glycerinated or carbolised vaccine be employed."

b) *Canine* Inasmuch as human

rabies in this country usually comes from the bite of a rabid dog, quite as important as treating a human case is the prevention, if possible, of rabies in dogs. Special vaccines, made by the Semple method, are being strongly advocated for the routine immunization of dogs, and some health officials would make their use compulsory by law. Unfortunately these vaccines frequently fail of their purpose, because dogs given one, two and three injections of the carbolized vaccine have later developed rabies, and, sometimes because of their owners' feeling that the vaccine treatment had made rabies an impossibility, diagnosis has been delayed and the animal has been allowed to be a menace until the symptoms became unmistakable. Reference to Semple's original article should convince one that a single injection, or even two or three injections of such a vaccine can hardly be counted on to make dogs invulnerable to the disease.

15 *Rocky Mountain Spotted Fever* The Federal Public Health Service has announced that a vaccine against this disease may be obtained free of charge by application to the United States Public Health Service Laboratory at Hamilton, Montana. Ranchmen, prospectors, and students investigating this disease can now protect themselves against this infection.

#### 16 *Scarlet Fever Streptococcus Toxin*

a) *For the Dick Test* Recent improvements in the preparation of this product in broadening its polyvalency by including the toxins of more strains of scarlatinal streptococci, by increasing the amount of toxin for the skin test dose and by



buffering the toxin dilution, thus making it more stable, have all operated to increase the reliability of the Dick test. This toxin can, therefore, be used with greater assurance than heretofore that a positive reaction to the test indicates susceptibility to the disease—a negative reaction, insusceptibility.

b) *For Active Immunization*

These improvements in the preparation of the toxin, and modifications in the manner of its administration enhance the value of this product for prophylactic purposes. The Dicks now recommend a graduated series of five injections of 500, 2,000, 8,000, 25,000 and 80,000 skin test doses of toxin at weekly intervals. Such a course is claimed to produce an immunity to scarlet fever in over 95 per cent of those so treated and one which persists for at least three years. The schedule of Young, consisting of bi-weekly injections of 500, then 3,500 and finally 25,000 to 30,000 skin test doses reduces the number of injections by two and appears to be equally efficacious. This toxin may sometimes give rise to a constitutional reaction, simulating the early symptoms of scarlet fever. To avoid such occurrences it is advised that castor oil be given before the injections which, furthermore, should be made when the stomach is empty. A second Dick test to determine the development of immunity should follow sometime after the last injection of toxin.

The application of the Dick test and active immunization to nurses and those likely to be exposed to scarlet fever has proven a successful way of protecting them. On account of the present mildness of the disease and the

long series of test and immunizing injections, it is questionable if it is profitable to extend this method to larger groups such as institutional or school children.

17 *Smallpox Vaccine Virus* The first vaccine to be discovered, and the one longest and most extensively used, vaccine virus stands as one of the most valuable immunizing agents man has yet devised. Immunologically considered it should be an efficient prophylactic. Being the living virus of vaccinia or cowpox it is closely related to the virus of variola, and it creates much the same train of physiological processes that operate in a mild case of smallpox, resulting in a prompt and more or less lasting protection against that disease. Being a living virus it should be given all the care in preservation and handling that its manufacturers bespeak for it. Fresh lots only should be used and they should be kept continuously at a temperature below 5° C. Again quoting from a previous paper by the author, "In order to obtain the best results, strict attention should be paid to the method of vaccination which is described in the leaflet accompanying each package of the vaccine distributed by the Massachusetts Department of Public Health, and which has also been published by Leake and by White.

"The older methods of cross hatching, incision and linear scarification should be abandoned, and the simple, painless and wholly satisfactory technic of multiple pressure be used instead. The method of single or multiple puncture is not to be recommended because recent reports show that undesirable results may follow. Vaccina-

tion by intradermic injections, as lately advised by Toomey and Hauver, holds dangerous possibilities and should not be used.

"When vaccinations are performed by the multiple pressure (Kinyoun) method, no dressings should be applied to the vaccinated site and under no circumstances should shields or tight bandages be applied. Shields are an abomination and their manufacture should cease. Vaccination should always be performed on the arm and never on the leg. If any untoward reaction occurs, if the vesicle or pustule is injured or broken, or if the scab comes off prematurely, the vaccination wound may be painted with tincture of iodine or a 4 per cent alcoholic solution of picric acid, which if applied more than 48 hours after vaccination will not interfere with the development of immunity. Then such care as is indicated should be promptly given.

"Too great stress cannot be given to the importance of vaccination technique. Fresh virus, applied by the multiple pressure method will give a maximum of "takes" in first vaccinations, a maximum of accelerated "takes" or immune reactions in revaccinations, with a minimum of discomfort and undesired results.

"Careful attention, especially in revaccinations, should be given to the appearance of vaccinoid or accelerated "takes," and of immune reactions. The vaccination site should, therefore, be observed on the third day and twice later, usually four and eight days after vaccination. The various reactions following vaccination have been excel-

lently described by Hooker and also by Leake.

"The ideal plan for vaccination is to vaccinate babies during their first year of life and again before entering school. During epidemics and where definite exposure is known to have taken place revaccinations should be performed.

"Smallpox vaccines, other than the present dermo-vaccine obtained from calves have been put forward with claims of superiority. The testicular vaccine of Noguchi, the neuro-vaccine of Levaditi and various vaccines treated with a variety of chemical agents have been tried and some of them are in use in different parts of the world. They appear to possess no distinct advantages over the calf vaccine and at present are not to be recommended."

18 *Staphylococci* Ever since Wright's first treatises on bacterial vaccines, those made from staphylococci, particularly the albus and aureus, have been considered as having definite therapeutic worth for treating and preventing the recurrence of local infections due to these organisms. In the case of furuncles, carbuncles or other abscesses, vaccine treatment seems to hasten maturation and healing. In the indurated or burrowing infections so typical of *S. aureus*, persistent treatment preferably with an autogenous vaccine often checks the progress of the disease and prevents relapse. In septicemia due to these cocci it is difficult to see why the introduction into the already infected body of additional cocci, even though killed, should benefit the condition. It has been claimed that in such cases the

septicemia has been aborted or that sterilization of the blood stream with localization of the infection has taken place. But such sometimes is the course of general sepsis under merely supportive treatment.

19 *Streptococci* The immunologist looks for a definite but not marked immunologic response on the part of a body injected with killed streptococci, a response specific for the biologic groups administered and sometimes specific only for single strains. Streptococcal infections of the sinuses, the middle ear, mastoid process and endocardium have generally been found to resist vaccine treatment, and what has just been said about staphylococcus septicemia applies equally well to sepsis with streptococcus. Where it is desired to prevent secondary infection from these cocci the use of a vaccine of wide polyvalency might result in some basic immunity. However, in using such a vaccine one should bear in mind these limitations.

20 *Tuberculin and "B C G"* For revealing the existence of tuberculous infection the intradermal injection of Old Tuberculin ("O T") by the method of Mantoux is our most discriminating test, although as in other tuberculin tests, a positive reaction may mean either healed infection or active disease. As the incidence of tuberculosis continues to decline, and as opportunity for infection decreases, this test will acquire greater and greater clinical significance. For the treatment of tuberculous disease Old Tuberculin, Bouillon Filtrate ("B F") and the Bacillus Emulsion ("B E."), used singly or in combination should suffice so far as antigenic spread is

concerned. Ophthalmologists, almost universally, prefer the Tuberculin Residue ("T R"), which has much of the antigenic value of "B E." without some of its disadvantages.

The medical world is now engaged in discussing Calmette's "B C G" as an immunizing agent against tuberculous infection. This preparation is made from a living culture of a strain of bovine tubercle bacillus degraded in virulence by long, successive cultivations in a bile-containing medium. Calmette claims that, being robbed of its virulence and invasiveness, it produces a benign local lesion which stimulates anti-tuberculosis immunity. It is given to infants by mouth in the first days of life, or it may be given subcutaneously. Extensive clinical studies have been under way in Europe for some years and if the statistical data could be taken at their face value, it would appear that children and also young cattle treated with "B C G" have escaped tuberculous disease in far greater proportion than their unvaccinated neighbors of corresponding ages. Petroff, however, has challenged the harmlessness of this vaccine and reports that he has dissociated this culture into both virulent and non-virulent strains. This possibility has been denied by French workers but until this very important question is decided, it would seem wise to be cautious. From what we already know of immunity in tuberculosis, such a vaccine, even if it is innocuous, and even if it should be absorbed from the intestinal tract and find lodgement in a lymph node setting up a localized tubercle, would at most bring about only a low grade immunity to infection.

by the tubercle bacillus. Such a scant, acquired resistance may augment the body's natural defenses sufficiently to retard extension of the infective processes, but until more convincing evidence appears and until the children already vaccinated reach the age of greatest vulnerability to tuberculous disease any dogmatic opinion may wisely be withheld.

21 *Typhoid and Paratyphoid Bacilli* Among the first bacterial vaccines to be devised, vaccines made from the typhoid bacillus and lately from this bacillus combined with *Salmonella paratyphi* (B paratyphosus A) and *S. schottmulleri* (B paratyphosus B) have more than justified their early promise. Absolute immunity to typhoid and paratyphoid infection does not result from the usual course of three injections, nor does this immunity persist for any great length of time, yet one series of three injections usually protects against any but a massive infection, and this protection can be continued by yearly injections where the typhoid hazard is great, or by bi- or tri-yearly injections where the chance of exposure is no greater than that confronting those who care for the sick. By injecting in divided doses at weekly intervals until a full two and one-half cubic centimeters are given, both local and constitutional reactions in adults may be avoided. Besredka advocates the administration of such vaccines by mouth, not only for the purpose of avoiding reactions, but more especially for the theoretical purpose of applying the immunizing antigen directly to the tissue liable to infection. This idea may appear fantastic or not according to one's view-

point. Recent experimental studies show that specific agglutinins, precipitins and complement-fixing antibodies appear in the blood of persons to whom the triple typhoid-paratyphoid vaccines have been administered orally, arguing therefore for the creation of an active specific immunity. Those so-called "Entero-vaccines" are offered by many of the European laboratories, but in this country we have been content to wait until further favorable information is forthcoming.

22 *Other Vaccines* The above list, while incomplete, includes the preparations that are most commonly used. Manufacturing laboratories in various countries supply vaccines or similar products for the prevention and treatment of asthma, erysipelas, ozena, pyorrhoea, rheumatism, rhinoscleroma and other conditions, infectious and otherwise. Since to these products it is not possible to apply our present standards of appraisal, they may be left out of consideration.

#### SUMMARY

If we disregard those vaccines which fail to reach our standard of evaluation based either on scientific measure or on the result of reliable and controlled clinical experience, the list dwindles. There is left, however, an array of products of incalculable worth for the prevention of infectious disease. It would seem from the answers to Hektoen's questionnaire that physicians out of their personal experience, are practicing a somewhat similar process of elimination. With the passing of fads, by the application of strict criteria, and after the further accumulation of clinical results, some

of the preparations now on the market will fall into disuse, with a gain to the patient in accuracy of diagnosis and soundness of treatment

## II SERUMS

In appraising serums on the basis adopted in discussing vaccines we can prophesy what their general physiological action will be and, with far greater conciseness than is possible in the case of vaccines, just what immunologic effect to anticipate. Knowing that serums may contain approximately from six to eleven per cent of proteins (globulins and albumin) and that concentrated serums may contain from ten to nineteen per cent of globulins, and knowing the allergic status of the recipient we can usually foretell the constitutional response to their injection and avoid many of the disturbing reactions that follow their administration to serum-hypersensitive persons. There still remains the little-understood realm of the non-specific stimuli of which serum proteins are capable. In the case of immune serums, close acquaintance with what we may call the philosophy of the disease coupled with familiarity with the immunologic nature and antibody content of the antitoxic or antibacterial serum will indicate beforehand the possible value of the treatment in any given case. Such knowledge teaches us the limitations as well as the applications of this class of biologic products. Stated in general terms, a potent serum corresponding immunologically to the infection to be treated, given in sufficient dosage early in the disease should, if no serious complicating factors exist, be of the greatest aid in bringing about recovery. The value of

the serum will decrease as the dose is diminished from the proper level or as the disease progresses. It should be borne in mind that the injection of foreign protein, especially in the amounts represented by the average serum dose, alters the individual's physiological response to subsequent injections of a similar protein. For this reason the free use of antitoxic or other serums, unless the condition strongly warrants their administration, should be deprecated. It should be further remembered that the passive immunity conferred by heterologous immune serums is of short duration, lasting only some two weeks or more and that the period of protection is even shorter in the case of patients who at some previous time have received injections of horse or other foreign serum products. So, too, will the time of appearance and the level and persistence of the immunity depend upon the route of administration. For a further understanding of the curative value of this class of products it may be mentioned that with most antitoxins, laboratory tests give an accurate estimate of their actual immunizing value, but with antibacterial serums the parallelism is by no means so close. This is because of the difficulty of reproducing in suitable experimental animals such infectious diseases of man as pneumonia or meningitis, although such toxemias as diphtheria and tetanus may be approximated closely enough in guinea pigs and other common laboratory animals.

I *Antianthrax Serum* When the anthrax lesion is in the skin and underlying tissues the prompt and intelligent use of surgery is often sufficient

When such an infection has progressed, or when it exists in the lung or alimentary tract the use of anti-anthrax serum will reduce the chances of a fatal outcome. Fortunately, such a serum is now available and should be used according to directions in all infections due to the anthrax bacillus.

2 *Anterior Poliomyelitis* The rationale for the use of convalescent serum in this disease appears to be sound. Recovery from an attack brings a life-long immunity, the serum from a recovered patient neutralizes infectious brain and cord *in vitro*, and it protects monkeys against what would otherwise be a fatal dose of such virus. Now that some monkeys, especially *Macacus rhesus*, can be infected with poliomyelitis virus by injecting them with the brain or cord from a human case, the way has been opened for testing human convalescent or other serum for protective action. Both Flexner and Aycock with this method have shown that the blood serum of many adults contains substances antagonistic to the virus, while the serum of persons convalescent from poliomyelitis has such an appreciable protective action that one would expect such a potent serum given early and in sufficiently large doses would stay the course of the disease. While the results following treatment of sporadic cases can be considered as being no more than suggestive, Aycock's analysis of the results of the Massachusetts cases treated in 1927 and 1928 gives us the first statistical evidence of the benefits of this form of treatment. When the serum was given in the first stages of the disease before serious cellular impairment had taken

place recoveries and freedom from crippling sequelae were far more frequent than was the case of patients who received no serum. From the very nature of this disease with the damage to the cells of the brain and cord, one would expect that this serum would be of value only in preventing further development of the infectious process and would have little or no curative action in remedying any cellular impairment already present. Early diagnosis and prompt treatment, therefore, are essential if any measure of success is to be expected. For the preparation of this serum, the blood should be drawn if possible from a person convalescent from poliomyelitis, the serum separated, clarified and tested for potency and for sterility, and then injected into the patient both intraspinaly and intravenously. Aycock advises that about 15 to 20 cubic centimeters of the serum be administered by the spinal route and twice the amount into a vein.

Serums produced by the artificial, active immunization of horses with streptococci have been tried and claims made of therapeutic efficacy, yet when tested for virucidal action they have been found lacking in protective power.

3 *Antidysentery Serum* Polyvalent serums made by actively immunizing horses with the Flexner, Shiga and other strains of the dysentery bacillus are useful in the treatment of bacillary dysentery only, and their value varies in inverse ratio to the length of time that has elapsed since the onset of the attack.

4 *Anti-gas-gangrene Serum* Because the bacteria causing this type of

infection, such as *Clostridium welchii*, *Cl oedematiens*, *Cl oedematis-maligni* and others, produce their characteristic effects through the toxins they elaborate, the treatment of these conditions with a serum containing specific antitoxins is logical. Such antitoxic serums are obtainable from a few of the manufacturing laboratories, and along with appropriate surgical measures are indicated in treatment.

5 *Antigonococcic Serum* Inasmuch as gonococcus apparently produces no soluble toxin, the most that could be hoped for in our present state of knowledge, would be the production of a serum containing antibacterial substances for this organism. While serums are available that contain specific agglutinins, complement-fixing and other antibodies, their immunologic reactions in vitro are not of a high order, and their therapeutic action is uncertain.

6 *Antimeasles Serum* Many and varied have been the bacteria that have been described as being intimately associated with measles if not the cause of it. Attention now, however, is almost entirely directed to the green diplococci first described by Tunnichliff, and the more or less similar streptococcus of Ferry and Fisher. These cocci have been found in the blood and throats of patients in the early stages of the disease. So far as can be discovered from the literature the critical test for etiological relationship by producing the disease in a susceptible person by inoculation with a pure culture has not been tried. Under suitable cultural conditions these cocci have yielded a toxin which is said to have the same relation to measles immunity

as does diphtheria toxin in the Schick test or scarlet fever streptococcus toxin in the Dick test. This extracellular toxin is neutralized by the serum of measles convalescents.

These facts warrant the attempt to prepare an artificial immune serum as well as support the use of convalescent serum for prophylaxis. Tunnichliff has, indeed, succeeded in immunizing goats to the toxin of her diplococcus, as proved by careful laboratory experiment, and, in the hands of Hoyne, Gasul and Halpern this immune goat serum has been found to prevent or modify measles in susceptible persons exposed to the disease. A similar serum has been obtained from the horse by Tunnichliff and White, which in vitro compares favorably in its immunological behavior with immune goat or convalescent serum. Further clinical trial is necessary before passing judgment on these new products. While there is ground for hope that such serums may protect temporarily against infection or mitigate the disease when given in the prodromal period, there is no indication that they would be of any avail in treatment.

Degkwitz believes that measles is caused by a filterable virus, often associated with a green-producing coccus. He claims to have cultivated this virus and with it has produced an immune serum from the sheep. This serum has been put to clinical trial, but the reports are contradictory.

"Convalescent serum, however, (to quote once more from a previous discussion) may be accepted as a valuable agent in preventing measles, or better for modifying an attack so that the patient while being spared any harmful

effects of the disease is permitted to develop an active and presumably lasting immunity

"There are difficulties in obtaining an adequate supply of this convalescent serum, but the difficulties are not insuperable unless large numbers of exposed persons are to be treated. The blood should be taken only from individuals who are definitely known to have had measles and then as *soon after convalescence* as possible. Should such a source of supply be lacking the blood of persons with a history of previous measles may be used. The usual strict precautions to be observed in the case of all human serums, such as the donor's freedom from communicable disease, and the sterility of the serum, should be observed.

"Richardson and Jordan advise a dose of from 6 to 10 cubic centimeters, given intramuscularly. When injected within the first four or five days after exposure (counting two days additional from the date of the appearance of measles in the person to whom the contacts were exposed) the disease is usually prevented. When given later this dose generally prevents a severe attack but may allow a mild form of the disease to develop, which establishes a lasting active immunity. The dosage cannot be accurately determined because serums vary in their protective power. The age and size of the person receiving the serum also influence the amount to be injected. In general, it may be said, that at the present time convalescent serum is a valuable agent for protecting young and susceptible children against a malady, which without the serum may cause harmful and sometimes fatal results."

7 *Antimeningococcic Serum* A former discussion of this serum by the author may be repeated here. "In epidemic cerebro-spinal or meningococcus meningitis the use of antimeningococcic serum has brought about a marked reduction in fatality and in the physical damage that follows such infections. Its administration is indicated in every case of meningitis due to meningococcus and may be given to advantage in many cases before a definite bacteriologic diagnosis has been established. All such serum produced in laboratories under the supervision of the United States Hygienic Laboratory is polyvalent, and contains antibodies for strains of the various agglutination and tropin groups. It should always be administered subdurally and at the earliest possible moment. When injected into the spinal canal the dose should be slightly smaller in amount than the spinal fluid withdrawn, and it should be injected slowly and under gravity pressure—not by syringe.

"The serum may also be injected into the ventricles, but this route is not commonly chosen except in severe or obstinate cases. Its injection into the *cisterna magna* is comparatively free from danger and is recommended by Ayer and others, particularly in child patients. The intravenous injection of the serum, advocated by Herrick and others, may be of benefit but theoretically at least, only in early stages of the disease. Directions for continued serum treatment can be found in text books and in circulars accompanying the product.

"The practitioner should bear in mind that from year to year or where the infection is brought from other



countries, the strain or strains of meningococcus causing the infection may be of a type not covered by the usual serums. In every case of meningococcus meningitis, wherever possible, the organism present in the spinal fluid should be isolated and carried under cultivation. Then, should the patient fail to respond satisfactorily to treatment with the particular preparation used, it may be possible by simple agglutination tests to select another lot or make of serum which will have a higher antibody content for the strain involved. The serum treatment of meningococcus meningitis should, therefore, always be accompanied by careful bacteriologic and serologic control."

8 *Antiplague Serum* The plague bacillus is notable for the highly poisonous nature of its protoplasm and for the severe toxic effects that accompany the disease in man. In preparing a therapeutic serum, therefore, the plan of immunizing horses is to develop both antitoxin and antiendotoxin. The method of Yersin is the one employed in making this product. Rosenau says of the Yersin serum, "At most this antitoxic serum is weak, it has feeble and transient protective properties, and doubtful curative power. Very large quantities must be administered in the disease to obtain any effect at all."

9 *Antipneumococcic Serum* Long-continued laboratory study has proved that the introduction of dead pneumococci (of Types I and II, at least) into the animal body leads to an active immunity as shown both by resistance to subsequent infection and by the presence of agglutinins, protective and

other antibodies in the serum of such an animal. With due allowance for its limitations it can be said that antipneumococcic serum, Type I, prepared according to the original or modified method of Cole, administered in full doses within the first three days of the attack frequently checks the disease and reduces its fatality. Antipneumococcic serums for Type II, III and IV infections has been found to be clinically valueless, a fact which squares with laboratory experience. By improving the methods for horse immunization and by separating out and concentrating the protective substances, preferably by the method of Felton or that of Banzhaf, we now have "Pneumococcus Antibody Solution," which in the hands of Cecil, Park, Bullowa, and Lord, among others, has shown definite curative action in cases of Type I lobar pneumonia and a somewhat less but still favorable effect in Type II infections. In pneumonias due to pneumococci of Types III and IV, this antibody solution has been of very doubtful benefit. The lessening of the number and severity of attacks of serum sickness is one of the gains accruing from the concentration process. This remedy is still on trial but is now procurable in the market.

10 *Antirheumatic Fever Serum* Experiences of the past year have brought nothing to modify the author's earlier opinion, "Although some late publications, notably those of Small and of Birkhaug, give the idea that the riddle of rheumatic fever is solved, the solution is neither so simple or sure. Here it is claimed that a particular coccus is the cause of the disease and its train of distressing and

obstinate symptoms. A toxin is said to have been produced which, used in intradermic tests, denotes susceptibility or immunity to the disease, but the evidence is neither clear nor convincing. Here, too, an immune serum has been obtained about which widely diverging reports are heard. It is by no means certain that "*Streptococcus cardioarthritidis*" is the cause of rheumatic fever, and we must await the results of further investigation before passing judgment on the biologic agents now available."

11 *Antistaphylococcus Serum* Although Parker and others have demonstrated toxin production by staphylococci, the serums at hand are essentially antibacterial in nature. One would expect no more of them in the way of curative action than from antionococcic serum.

12 *Antistreptococcic Serum* Postponing for the moment any discussion of the streptococcal antitoxins, antibacterial serums specific for streptococci may be considered. These are made for treatment of infections due to *Streptococcus hemolyticus* and also *S. viridans*. From our knowledge of antistreptococcal immunity in general we would rate these serums low in immunizing value. The occasional favorable reports from their users encourage their continued manufacture.

13 *Antivenoms* Antiserums specific for venoms of the American rattlesnake, copperhead and water moccasin are now manufactured in the United States. Laboratory trials show that such serums not only neutralize these venoms in the test tube but protect animals injected with killing amounts of venom. When injected into human

beings bitten by any one of these three poisonous snakes, if given soon after the bite is received, they prevent or modify the toxic symptoms. The shorter this period the more useful is the antivenin. In other lands various institutes and manufacturing laboratories prepare similar products specific for the venoms of the various snakes native to the country.

14 *Diphtheria Antitoxin* This product is one of the greatest achievements of applied immunology. Higher than ever in antitoxic content per given volume, more stable and freed to a larger and larger extent from non-antitoxic proteins, it remains a sovereign remedy for diphtheria. Here again early administration enhances its value. The accepted but not always practised modes of administration are intravenously in the severest cases, intramuscularly in mild and also possibly a part intravenously in moderately severe infections, but subcutaneously only for prophylaxis. From the experimental work of Schick there would appear to be no advantage in giving more than 500 units per kilo of body-weight in the severer cases, and this amount corresponds to the maximum dosage recommended by Park and the manufacturers of this product. Any hesitancy about dosage should be dispelled by decision to administer the higher amounts recommended. Any suspicion that the patient is suffering from diphtheria demands the immediate injection of antitoxin in full dose without waiting for a bacteriologic report.

The prophylactic use of diphtheria antitoxin is decreasing. It is now preferred to perform Schick tests on

persons exposed and to take nose and throat cultures. When the reaction to the Schick test and the result of cultural examination are negative the individual is released from observation, where the Schick test is negative and the culture positive the person is considered as a carrier, where the Schick test is positive and the culture negative, daily cultures and clinical examinations are made, where both the Schick test and culture are positive a dose of 1,000 units or more of antitoxin should be given

15 *Erysipelas Antitoxin* The facts that hemolytic streptococci are intimately concerned in this disease, that these cocci produce a toxin analogous to that elaborated by scarlatinal streptococci, and that erysipelas is essentially a toxemia, would seem to furnish a basis for antitoxic therapy Amoss and also Birkhaug have developed such antitoxins, which are now supplied in concentrated form, and clinical reports of the results following their use are mainly favorable The close relationship of streptococci of the erysipelas group to those of the scarlatinal group would seem to be ground enough for employing polyvalent scarlet fever streptococcus antitoxin in the treatment of erysipelas The English follow this view as does also McCann, apparently with satisfaction On these grounds, therefore, it might be predicted that scarlet fever streptococcus antitoxin might or might not be of benefit in erysipelatos conditions. The protection afforded is temporary and should not be expected to prevent relapses

16 *Scarlet Fever Streptococcus Antitoxin* The potency and the immun-

izing compass of this product have been increased by the addition of different toxigenic strains of scarlatinal streptococci to the antigens used for immunizing the producing horses, by improvements in the scheme of injection and by refinements in the concentration process The methods for testing the potency still leave much to be desired, but manufacturers obviate this difficulty by recommending an amount which is usually sufficient for the case This antitoxin given in adequate amounts early in the disease reduces the toxemia in a gratifying way, and the greater the toxemia (in early cases) the more striking the effect Since it is essentially an antitoxin one would not anticipate that it would prevent the development of septic complications, except in so far as it, by lessening the debilitation of the patient, might raise the general level of resistance to further invasion by this streptococcus Some authors recommend its use in all cases of scarlet fever while others would limit its use to the moderately severe and severe cases

The prophylactic use of this antitoxin does not seem indicated unless exposed persons are to be away from daily medical observation The disease usually attacks only about one in ten of those exposed, the antitoxin confers passive immunity for a matter of only two weeks or slightly more, while the source or sources of infection may continue to be present and cause this fever in exposed persons in whom this passive immunity has disappeared Then second or subsequent injections of this product may be followed by serum sickness The daily inspection

of contacts, with the immediate administration of the antitoxin at the first symptoms of scarlet fever, would in the main, seem to be the better practice

17. *Tetanus Antitoxin* Few biologic products have been subject to such trial as was given tetanus antitoxin during the World War. Out of that welter it was learned that a prophylactic dose of 1,500 units, administered shortly after the wound was received, would ward off tetanus if the wound were slight or required no further surgical interference. The protection was not sufficient, however, to prevent development of the infection in those cases requiring subsequent operation. It, therefore, became the rule to give antitoxin not only at the time of the wounding but before each surgical operation. This rule should hold in civil as in military life. For treatment the antitoxin should not be given grudgingly. It should be injected intraspinally at the earliest moment, and repeated frequently and in large doses. Administration by the venous route or into nerve sheaths is inferior in effect to injection into the spinal canal.

18. *Other Serums* In addition to the serums just discussed, there is normal horse or other animal serum for the arrest of hemorrhage and the treatment of burns as well as a number of analogous products which, because their merits can not be measured according to our chosen standards need not be included here. For example, in the catalogs of foreign manufacturing establishments one finds listed such products as coli-paracoli, grippe, ictero-hemorrhagica, leprosy, thyroid, ty-

phoid, uremia and vaccinia antisera, all of which under the ruling of the United States Hygienic Laboratory would be classed as products for which no standard of potency exists.

#### SUMMARY

With these theoretical considerations the clinician should neither expect nor demand that immune sera do more in controlling the diseases for which they are intended than the immunologist may honestly predict for them. Bearing in mind that serums represent proteins foreign to the human body, the prudent physician will determine the allergic condition of his patient before such treatment and be ready with epinephrine to combat any untoward reaction following serum injections. For the same reason such a physician may spare his patients the possibility of future serum sickness by not giving serums needlessly. Here, and on this account even more caution is demanded than in the use of vaccines.

Fresh and potent serums, and only those of proven value, given early in the disease and by the most favorable route, continue to be the physician's greatest and sometimes sole aid in curing some of the more malignant infectious diseases.

This critical review of serums and vaccines must be taken as of today. The development of non-specific biologic therapy, the perfection of new methods of serum and vaccine production and the discovery of other agents of this kind will necessitate new or revised appraisals. Disappointments will be fewer if general use waits upon theory, upon laboratory experiment, and upon controlled clinical observation.

# The Diagnosis of Gonococcal Arthritis With Report of Three Cases in Patients With Chronic Rheumatic Endocarditis\*

By O H PERRY PEPPER, M D, *Philadelphia*

NOT so many years ago the term gonococcal arthritis connoted an ankylosing monarticular process, today we know that gonococcal arthritis is usually a polyarthritis which may so closely simulate rheumatic fever as to lead to diagnostic error unless one is constantly alert to suspect and search for the evidences of gonococcal infection

We have also learned that all prostatitis is not gonococcal nor need it have even started as such, and we have gained a hearty respect for both venereal and non-venereal prostatitis as a focal cause of such distant troubles as arthritis, iritis and neuritis

Notwithstanding these advances, it seems to me we are still far from appreciating both the frequency with which neisserian infection is responsible for arthritic phenomena and the difficulties of recognizing this factor when it occurs

Impressed with this view, we have attempted for the past few years to make sure that the possibility of gonococcal infection was carefully investigated in every patient with acute or chronic arthritis, including even ap-

parently typical rheumatic fever, admitted to the adult medical service at the Hospital of the University of Pennsylvania. As always happens when such a state of mental "sensitization" exists, more instances of the disease in question were discovered. After careful investigation a number of cases of supposed rheumatic fever proved to be gonococcal arthritis and among the infectious arthritis group a greater percentage were attributed to gonococcal infection. For example, during 1928, among 46 cases of arthritis there were 20 in which investigation supported an initial suspicion of gonococcal etiology, and further study resulted in 14 of these 20 being finally so diagnosed. I have no desire to present any statistics but merely to report some of our experiences and conclusions

At the start let me emphasize the difficulties inherent to the making of the diagnosis of the gonococcal nature of an arthritis. Only when an acute arthritis develops during acute gonorrhoea can one safely and easily make this diagnosis. Under other circumstances, it is usually made with difficulty and doubt. Even the discovery of a gonococcal infection does not prove its causal relation to an existing

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arthritis any more than does the finding of a peridental abscess. Furthermore, the tendency of the gonococcus to die out and leave only a secondary flora as evidence of a former gonorrhoea in both males and females adds to the difficulty.

The uncertainty is in a large measure due to the fact that all the diagnostic criteria which can be routinely used are far from satisfactory. They include the history, the character of the arthritis, other clinical features, the complement fixation test, roentgenology, joint puncture, the course of the disease and the results of treatment. Let us briefly discuss each of these.

*History* Both the previous medical history and the circumstances immediately preceding the onset of the arthritis are important and yet may be very deceiving. When a clear story of gonorrhoea is obtained it must obviously arouse suspicions that a subsequent arthritis may be gonococcal, even though a story of joint injury is obtained. Frequently injury seems to determine the onset and the localization of a gonococcal arthritis. A negative history on this point is to be given no weight at all not only because venereal disease is often denied but because in the female its presence is often unknown. Far more significant in the female is the history of leucorrhoea, pelvic inflammatory troubles or some chronological relation of arthritis to marriage or to child bearing.

Among our recent cases are examples of each of these relationships, in one man three of five attacks of gonorrhoea were followed by arthritis. It is the rule that if gonococcal arthritis

is to occur in an individual it will usually appear with the first gonorrhoea and having once occurred will recur with each fresh gonorrhoea. In another, the entire sequence of gonorrhoea, polyarthritic stage, monoarthritis in sternoclavicular joint, and finally the typical painful heel of the os calcis spur could be elicited.

The patient's age at the onset of the arthritis must be given some weight, a very youthful onset, of course, argues against an arthritis being neisserian unless the case belongs in the fortunately rare infantile group. There is no question but that such cases do occur and Cooperman<sup>1</sup> has reported an epidemic with 44 such cases of gonococcal arthritis all in infants from the same hospital ward. Apparently infants readily develop gonococcal arthritis from very slight local lesions.

There may be no age above which a primary attack of rheumatic fever may not occur but a primary attack certainly becomes less common after the age of twenty. Similarly, the presence or absence of tonsillitis, growing pains, chorea or rheumatic heart disease would seem to be of importance in the history. This question will be referred to later and several cases reported to illustrate the difficulties.

It has usually been agreed that gonococcal arthritis is far more common in males than in females. Thomas<sup>2</sup> had 97 males and but 10 females in his recently reported series but it is doubtful whether this expresses the true proportions. The recognition of

<sup>1</sup>Cooperman, M B. *Am J Dis Child*, 1927, 33, 932.

<sup>2</sup>Thomas, B A. *J Am Med Assn*, 1927, 89, 2147.

chronic gonorrhoea is far more difficult in the female and the history far less helpful as a rule. In our recent cases, there were as many females as males

*Character of the Arthritis.* Emphasis was first placed on the monarticular feature of neisserian arthritis, next on the tendency of the polyarthritis involvement to subside in all but one large joint, often the knee. Just as long as this criterion was demanded for the diagnosis of gonorrhoeal arthritis only such cases as exhibited these features were recognized as such and so diagnosed. Today it is accepted that the temporomandibular and sterno-clavicular joints are often involved in gonococcal arthritis, seldom if ever in rheumatic fever. Blake<sup>a</sup> in the best available article on gonococcal arthritis supports this view. Among our recent cases of neisserian arthritis, there were instances of involvement of each of these two joints while neither joint was involved in the non-gonorrhoeal group.

Nevertheless one cannot usually distinguish on the basis of the arthritic picture some instances of so-called neisserian arthritis from rheumatic fever; nor others from non-gonorrhoeal infectious arthritis. There is not enough difference in the onset, the order of involvement, the number of joints involved, those involved, the duration of individual joint involvement nor in the severity of the local symptoms to permit one to make a satisfactory differential diagnosis.

The phrase 'so-called neisserian arthritis' was used above with a purpose

<sup>a</sup>Blake, F. G. in Blumer's *Bedside Diagnosis*, Saunders, 1928

It is possible that we are trying to merge under this term two distinct forms of arthritis, one more acute and specifically due to the gonococcus often with that organism in the joint, the other arising no less from a focus containing gonococci but reacting to this focal infection in a non-specific manner. In the second type, although gonococci might be found in the focus there would also be a free flora of secondary invaders. In this form gonococci would not be present in the affected joints and the process would be chronic and not differentiable from a non-gonococcal infectious arthritis arising from a staphylococcal or streptococcal focus in tonsil or sinus. Strictly speaking these cases should not be termed gonococcal even though the initial infection was gonococcal and even though gonococci may still persist in the focus at the time of development of the chronic infectious arthritis.

In other words, even the finding of gonococci in what seems to be the causal focus of infection certainly does not prove that the arthritis, although due to that focus, is truly gonococcal. If we accept this view, it would explain many of our difficulties—the variations in the arthritic process, in the radiologic findings, in complement fixation of cases which we now attempt to include in one diagnostic group.

*Other Clinical Features.* Some authorities have stated that there are differences in the height of fever and its duration, in the sweating, in the leucocytosis or in the anemia. None of these criteria have seemed helpful to me.

Endocarditis is another matter and

its appearance during or soon after an arthritis argues strongly for a rheumatic process. Simple infectious arthritis seldom if ever has a cardiac complication while the rare instance of gonococcal endocarditis soon forces its diagnosis upon the physician. The same reasoning applies to pericarditis and even to myocarditis and disturbances of rhythm. One of our cases of arthritis strongly suspected of being neisserian developed a paroxysm of auricular fibrillation thus raising the interesting question as to how far this favored a diagnosis of rheumatic fever.

The leucocyte picture deserves mention. The leucocytosis will be high in acute purulent monarticular gonococcal arthritis but as a rule the leucocytosis will be greater in rheumatic fever than in polyarthritic neisserian arthritis. There is no difference in the range of the total white cell count between infectious non-gonococcal arthritis and gonococcal polyarthritis, nor do I give any weight to the claim that gonococcal infections are to be recognized by the occurrence of an eosinophilia. It is true that gonococcal pus often contains many eosinophils and it is probably from this that a circulating eosinophilia has been erroneously assumed. In none of our recent cases has there been an eosinophilia of more than 2 per cent, except one count which was 6 per cent of a normal total.

*Complement Fixation* It seems to be generally accepted that a negative reaction does not exclude the presence of a gonococcus infection, but that a posi-

tive test is certainly of value. Kolmer<sup>5</sup> claims that gonococcal arthritis yields from 80 to 100 per cent of positive reactions. During the past year in the cases of what we concluded were neisserian arthritis the complement fixation was positive in a little less than half. Among the negative cases were 3 in which gonococci were actually found, all of these negative cases were of long enough duration for a complement fixation test to have developed. The reaction does not become positive for a month and often not for six to eight weeks—a point not to be forgotten. One of the positive tests may have been due to vaccine given at a previous hospital, a possibility which also must never be forgotten.

*Roentgenologic Evidence* The X-ray Department of the University Hospital, under Dr H. K. Pancoast, recognizes two distinct joint pictures produced by gonococcal infection; the one is a chronic deforming arthritis with both hypertrophic and atrophic changes and is not to be differentiated as to cause from the roentgenogram alone. This corresponds to the non-specific form already referred to. Sometimes the presence of a spur on the os calcis will arouse suspicion. Baetjer especially emphasizes that long spurs are probably of gonococcal etiology.

The other form is an acute destructive process analogous to that produced by streptococci or pneumococci but a little less rapid. This picture occurring in a case lacking the history of a serious streptococcal or pneumococcal

<sup>4</sup>Mondor and Urbain. *Comptes rend Soc de Biol*, 1927, 96, 513 et al.

<sup>5</sup>Practical Text Book of Infection, etc., Saunders, 1923.



infection is strongly suggestive of a gonococcic etiology

Perhaps intermediate between these two is a rarer picture in which punched out areas occur in the bone underlying localized areas of involved cartilage; this resembles the picture seen in gout

Among 14 possibly neisserian cases, the X-ray supported the diagnosis in 8, of the other 6 one was a proved case of gonococcic infection but the X-ray was taken only 17 days after onset, far too soon to show any change, a second proved case had only synovitis, two were quite sure cases and might have been expected to exhibit suggestive changes but even on review did not, the other two were our least sure cases and the X-ray failure to assist added to our uncertainty

Reviewing these films brought out that much can often be learned by repeating the X-ray study after an interval of several weeks. The progress of the process was in several instances an important aid in diagnosis

While it is perhaps true as Baetjer and Waters<sup>6</sup> write that gonococcal arthritis does not present a distinct X-ray appearance, yet our experience would suggest that with the aid of a judicious use of the history the X-ray may be of valuable diagnostic assistance. Especially is this true if we distinguish between acute truly gonococcal arthritis and the other more chronic not strictly gonococcal process

*Joint Puncture* Our experience adds nothing to accepted views on this point. If the process be acute a cloudy fluid will be obtained which on stain-

ing will reveal many neutrophiles. Gonococci will usually not be found in the fluid, therefore one should search in the synovial membrane, taking a piece for biopsy.<sup>7</sup> When Gram negative diplococci, often intracellular, are found in stained spreads from an infected joint the organism is assumed to be the gonococcus. In the vast majority of instances this assumption is justified but it must not be forgotten that a monarthritides often of the knee, is not an uncommon complication of meningococcus infection and further that meningococcus bacteriemia occurs with little or no meningitis and finally that the meningococcus is a Gram negative diplococcus often intracellular and indistinguishable from the gonococcus by any staining method. There should be no opportunity for confusion in cultures. As an alternative to joint puncture a neighboring lymph node may perhaps be cultured. Forkner<sup>8</sup> successfully cultured gonococci from a lymph node from the axilla of a patient with a typical chronic infectious arthritis.

Axhausen<sup>9</sup> has recently pointed out that not all acute monarticular arthritis giving the picture of gonococcic arthritis is due to the gonococcus.

*Course of Disease and Results of Treatment* Attempts to draw diagnostic aid from the course of an arthritis have been unsuccessful with us. It is commonly accepted that the patient with rheumatic fever obtains more relief from salicylates than does

<sup>7</sup>Plisson, L. *Le Prog Med*, 1927, 42, 1543

<sup>8</sup>Forkner, C. E., *Bull Johns Hopkins Hosp*, 1928, 43, 257

<sup>9</sup>*Klinische Wochenschrift*, 1927, 6, 732

<sup>6</sup>*Injuries and Diseases of the Bones and Joints* Hoeber, New York, 1927

one with gonorrhoeal arthritis. This is in a measure true but it is hard to use this as a diagnostic criterion. Gonococcal polyarthritis may leave behind it just as little disability as does rheumatic fever but when gonococcal arthritis lingers in the knee or other large joint, ankylosis often results. Rheumatic fever does not produce ankylosis but acute infectious arthritis of any type may.

*Case Reports.* Each of the three cases to be briefly described presents gonococcal arthritis in a patient with an old rheumatic endocarditis. This coincidence raises some interesting questions. At first glance it would seem that evidence of a former rheumatic infection would argue that a subsequent polyarthritis would also be rheumatic. Such evidence might consist of a clear history of rheumatic fever in childhood, of repeated tonsillitis or chorea, or the discovery of a residual rheumatic endocarditis. Undoubtedly, as Torrey<sup>10</sup> has emphasized, an adult is far more liable to rheumatic fever if during childhood a previous attack of rheumatic fever has occurred. May it not be, however, that the same adult is rendered by the earlier rheumatic fever more liable to other joint affections as well as to further rheumatic fever? Blumer<sup>11</sup> has an editorial footnote on this point suggesting that a previous rheumatic fever makes the individual more subject to gonorrhoeal arthritis. The following cases suggest that this is so.

**CASE I** M H (1928-1147) A white, unmarried female aged 22 developed three months before admission, pain and swelling in the right elbow and knee. The knee recovered in one day, the elbow persisted, there was fever for two weeks.

After three months there was swelling and ankylosis of the right elbow and also limitation of motion in shoulder with considerable atrophy. Some involvement but to a less degree of the right wrist and hand. No other joints affected. The interne's tentative diagnosis was gonorrhoeal arthritis. Confirmatory evidence was obtained by the finding of gonococci in the vaginal discharge and by Dr. Pancoast's report that the roentgenologic appearance of the right elbow was strongly suggestive of gonorrhoeal arthritis.

Another side of the case, however, was presented by the finding of an undoubted mitral stenosis and of foci of infection in the tonsils, sinuses and mastoids. The mitral stenosis was in all probability an evidence of chronic rheumatic endocarditis even in the absence of any history of rheumatic fever or chorea.

Under thorough treatment all but the ankylosis improved and the case was sent for an arthroplasty.

**CASE II** M B (1928-879) a white married woman of 24 years of age was admitted with pain in the right elbow which had been present for one month. No other joints affected at the time but two years previously a sharp attack of polyarthritis.

The items suggesting a possible neisserian basis for the arthritis included a former salpingitis requiring operation, the presence of endocervicitis even though no gonococci were found, a strongly positive complement fixation and a roentgenologic suggestion of gonococcal arthritis.

On the other hand, the heart was enlarged to the left and a double murmur at the apex testified to mitral valvulitis with both stenosis and regurgitation. There was no history of any former rheumatic fever, chorea, or tonsillitis.

Nevertheless here again, we felt justified in the diagnosis of chronic rheumatic endocarditis and acute neisserian arthritis.

<sup>10</sup>Torrey, R. G. *Tice's System of Medicine*.

<sup>11</sup>Blumer, G. *Bedside Diagnosis*, Volume 1, p. 32, Saunders, 1928.

CASE III WB (1928-894) a divorced white male of 28 years of age had at 21 years his first attack of polyarthritis. During the following six years, he suffered six similar attacks each lasting from 3 to 6 months and involving an increasing number of joints. The attacks are worse in the winter.

In his earlier history there is no mention of rheumatic fever, chorea or tonsillitis. He admits gonorrhoea at 23, two years after his first joint attack.

On admission, the pain and stiffness involved the shoulders, knees, hips, sacroiliacs, both mandibular joints and the left sterno-clavicular. Physical examination revealed evidences of both aortitic and mitral valvulitis—presumably rheumatic in nature. The Wassermann was negative. The prostate was heavily infected but no gonococci were found. No suspicion of gonococcal arthritis was supplied by the X-ray. The complement fixation was positive, but this may have been due to vaccine given in a previous hospital.

In this case one must admit the old gonorrhoea and the persistent prostatitis but these do not prove the gonococcal nature of the arthritis. However, the involvement of the sterno-clavicular and temporo-mandibular joints would be adduced by some as suggesting a neisserian process.

All of these patients have been followed sufficiently long to exclude all reasonable possibility of the cardiac lesions being gonococcal in nature nor did they present in the hospital the evidence of this infection. It was formerly thought by some that gonococcal arthritis was often associated with a gonococcal infection of the

heart, which often was mild and recovered. This is no longer believed. According to our present views the above three cases are unquestionably instances of rheumatic heart disease. The absence of earlier rheumatic arthritis is interesting in that in its absence the joints would perhaps not have been expected to be peculiarly susceptible to later gonococcal arthritis.

*Summary* 1 Gonococcal arthritis is a frequent disease in both males and females.

2 It is protean in its manifestations and may closely stimulate rheumatic fever.

3 The true nature of a gonococcal arthritis will often be overlooked unless this etiologic possibility is kept constantly in mind.

4 Diagnosis of this condition is often difficult, the diagnostic methods unsatisfactory when used singly; combined they will usually prove sufficient.

5 It is suggested that a gonococcal focal infection may cause either a specific gonococcal arthritis or a non-specific infectious arthritis. Many of our diagnostic difficulties may arise from this.

6 There is some reason to believe that rheumatic infection prepares the soil not only for recurrences of rheumatic fever but also for other types of arthritis including the gonococcal.

# Complications and Sequelae of Chronic Ulcerative Colitis\*

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EVERY serious disease entails dangerous consequences, either during the progress of the illness or as a result of nature's effort to restore destroyed tissue. Particularly is this true of severe chronic infections. In the healing of tuberculosis formation of the scar may result in serious loss of function. Pneumonia through the sequel of empyema, not infrequently results in marked deformity of the chest. Another disease, hitherto thought of as a serious infection of the colon, has usually been considered without particular reference to its associated complications. There are few diseases more annoying or more severe in their course than chronic ulcerative colitis and, further, the conditions which this infection leaves in its wake are among the most distressing encountered in the practice of medicine. The conditions following, or closely associated with, chronic ulcerative colitis are multiple.

In a series of 693 cases of chronic ulcerative colitis examined at The Mayo Clinic in the five and a half years from January 1, 1923, to July 1, 1928, various significant complications and

lesions closely associated with the disease occurred as sequelae to or during the course of the infection. There were sixty-nine cases of polyposis of the colon, fifty-nine cases of stricture of the rectum or colon, thirty cases of arthritis, twenty-six cases of perirectal abscess, seventeen cases of cutaneous lesions, eight cases of nephrosis, or nephritis, seven cases of endocarditis, seven cases of splenomegaly, eighteen cases of perforation of the colon, fifteen cases of malignant disease, five cases of ocular disease, three cases of fatal hemorrhage, two cases of renal calculi, and one case of mesenteric thrombosis, and one case of tetany.

It must not be thought that each of the foregoing complications occurred in individual patients. Frequently multiple complications occurred in one case. One patient had with the colitis, endocarditis, arthritis, erythema nodosum, and iritis. The three conditions, chronic ulcerative colitis, arthritis and erythema nodosum, occurred together in several patients. Chronic ulcerative colitis, perirectal abscess and iritis occurred together. Perirectal abscess, polyposis and malignant disease occurred with chronic ulcerative colitis several times. Many other in-

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\*Read before the American College of Physicians, Boston, Massachusetts, April 8 to 12, 1929.

TABULATION  
DISTRIBUTION OF 268 COMPLICATIONS OCCURRING IN  
693 CASES OF CHRONIC ULCERATIVE COLITIS

Complication	Cases in which complications occurred	Per cent
Polyposis	69	10.0
Stricture	59	8.5
Arthritis	30	4.33
Perirectal abscess	26	3.7
Skin lesions	17	2.45
Renal insufficiency	8	1.15
Endocarditis	7	1.0
Splenomegaly	7	1.0
Perforation	18	2.6
Malignant disease	15	2.16
Ocular disease	5	.7
Hemorrhage (fatal)	3	.4
Renal calculi	2	.2
Mesenteric thrombosis	1	.15
Tetany	1	.15

stances of associated lesions could be mentioned. The fact should be stressed that complications do not preclude recovery from chronic ulcerative colitis.

In this series of cases multiple polyposis (fig 1) occurred as the most common complication. In a series of 117 cases studied by Logan in 1919 there were polyps in nineteen and in a later series studied, polyps occurred in twenty-six of 200 cases. Just as the disease, chronic ulcerative colitis usually begins in the rectum, so it is the most common site of origin of polyps. Later the number increases as they appear in the more proximal portions of the colon. That they originate during the progress of the disease has been repeatedly demonstrated. In the earlier stages of the disease the inflammatory phases so accurately described by Buie are seen. With the appearance of the larger ulcers between which are left islets of mucosa, there is a certain

heaping up of mucosa and apparent pinching off at the base so that two types of polyps may be differentiated easily: (1) a plateau-like excrescence appearing as definite mucosal hyperplasia, and (2) large pedunculated polyps which on section are found to be adenomatous polyps. If both of these occur extensively and are large enough to visualize by roentgenogram by barium enema, the prognosis may be grave. On the other hand, if limited to the field of the proctoscope they may be fulgurated and their potential danger becomes minimal.

Rectal stricture is the second most common sequel of chronic ulcerative colitis. In discussing stricture in this disease the reference is not to the ordinary narrowing of the colon which usually occurs after one or more attacks of ulcerative colitis. Interest is directed, rather, to localized regions of inflammatory and scar tissue which interfere materially with the passage

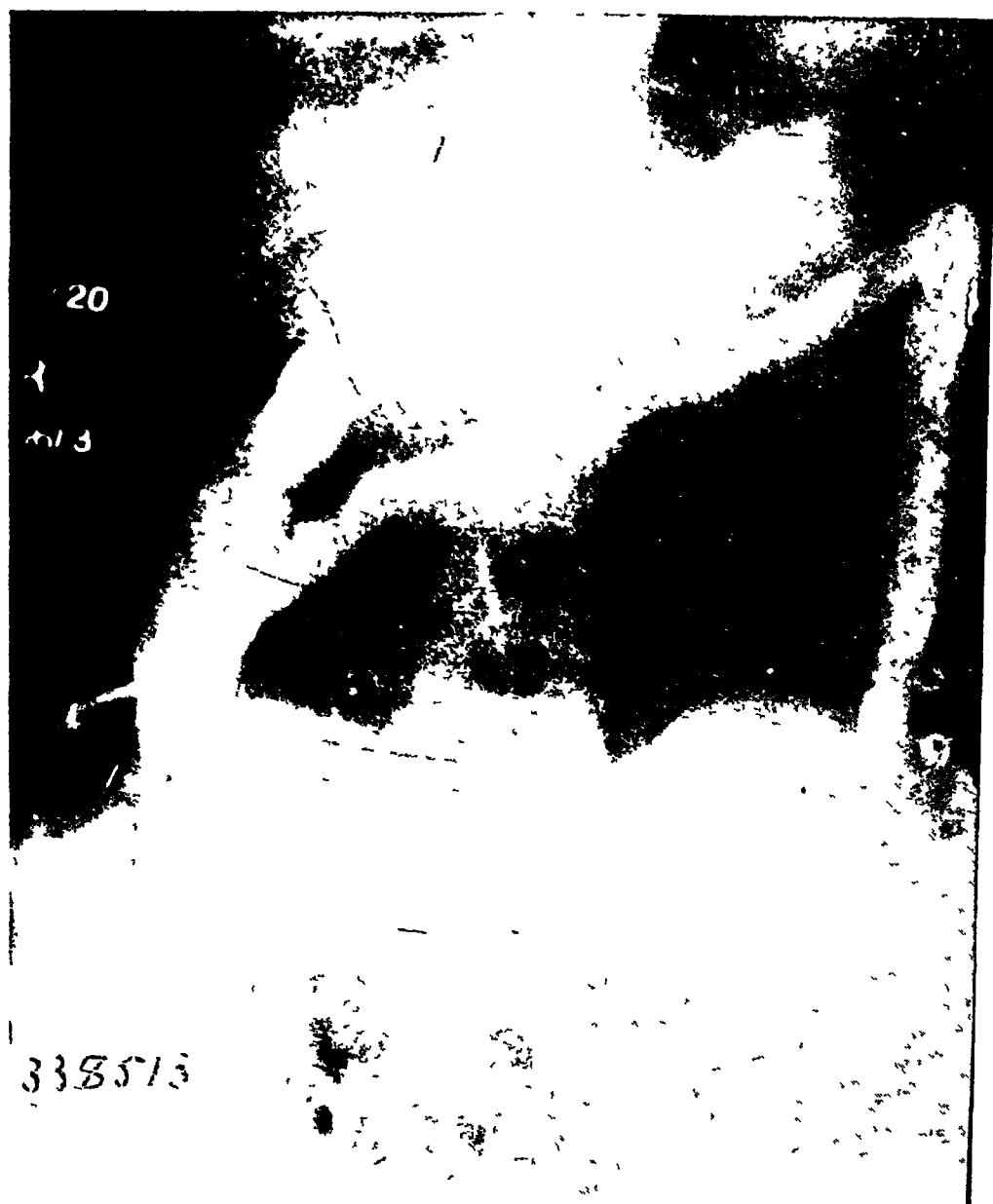


Fig 1 Colon after barium enema in a case of chronic ulcerative colitis and multiple polyposis

of the normal fecal current, thus inhibiting normal rectal function. In this series there were cases of multiple stricture in some of which the lumen was so narrow that pockets of pus would accumulate proximal to the stricture in various parts of the colon (fig 2). The commonest type of stricture, however, is a localized narrowing of the rectum on a diffusely narrowed base. These strictures are organic constrictions of the bowel to diameters as narrow as 0.5 to 1.5 cm, measured proctoscopically. The decrease in the relative number of such strictures as a complication is striking, in the years 1923 and 1924 stricture developed in 19 per cent of cases and in the next three and a half years, in only 6.3 per cent, a reduction by approximately 66 per cent. This can be attributed in part to newer methods of treatment.

Whether or not arthritis should be called a complication or an associated disease is a debatable question, but from the clinical standpoint it is generally considered to be a complication. In a large series of patients with chronic ulcerative colitis and arthritis in whom the diplostreptococcus of chronic ulcerative colitis was isolated from rectal lesions and injected intravenously into animals the lesions which resulted in animals were, as far as the rectum was concerned, in all essentials like the rectal lesions of patients, associated lesions in the joints, however, never have been noted in the animals. On the other hand, in a careful analysis of the histories of patients afflicted with chronic ulcerative colitis and infectious arthritis, various types of cases are noted. (1) those in

which each exacerbation of colitis is followed by a recurrence of the arthritis and in which, with improvement of the colitis, there is associated relief from the arthritis, (2) those in which the attack of arthritis may precede the colitis, and (3) those in which both disturbances occur in the same patient, apparently without relation. A further study of these cases is under way.

Perirectal abscess (fig 3) is one of the more serious, although fortunately uncommon, complications. Either one of the anal crypts becomes infected from the constant purulent rectal discharge or deep ulcers burrow beneath or to the side of the anal sphincters and point as one or multiple perirectal abscesses. From these abscesses, frequently, a pure culture of the diplostreptococcus of chronic ulcerative colitis is recovered. Conservative treatment in these cases cannot be urged too strongly. That there be the least possible surgical interference is most important. If the usual radical incision and drainage is carried out, most unfortunate perianal spreading of infection and functional anal deformity may result.

Perforation of the colon (figs 4 and 5) is another extremely serious condition which occurs in the more extensive and severe cases of chronic ulcerative colitis. Its incidence has been discussed elsewhere<sup>3</sup>.

Any discussion of an inflammatory disease of the colon would seem incomplete without reference to the lesions that occur in the skin. In this series these lesions included erythema nodosum, erythema induratum, chronic eczema, eczematoid and vegetative dermatitis, hemorrhagic purpura, ir-

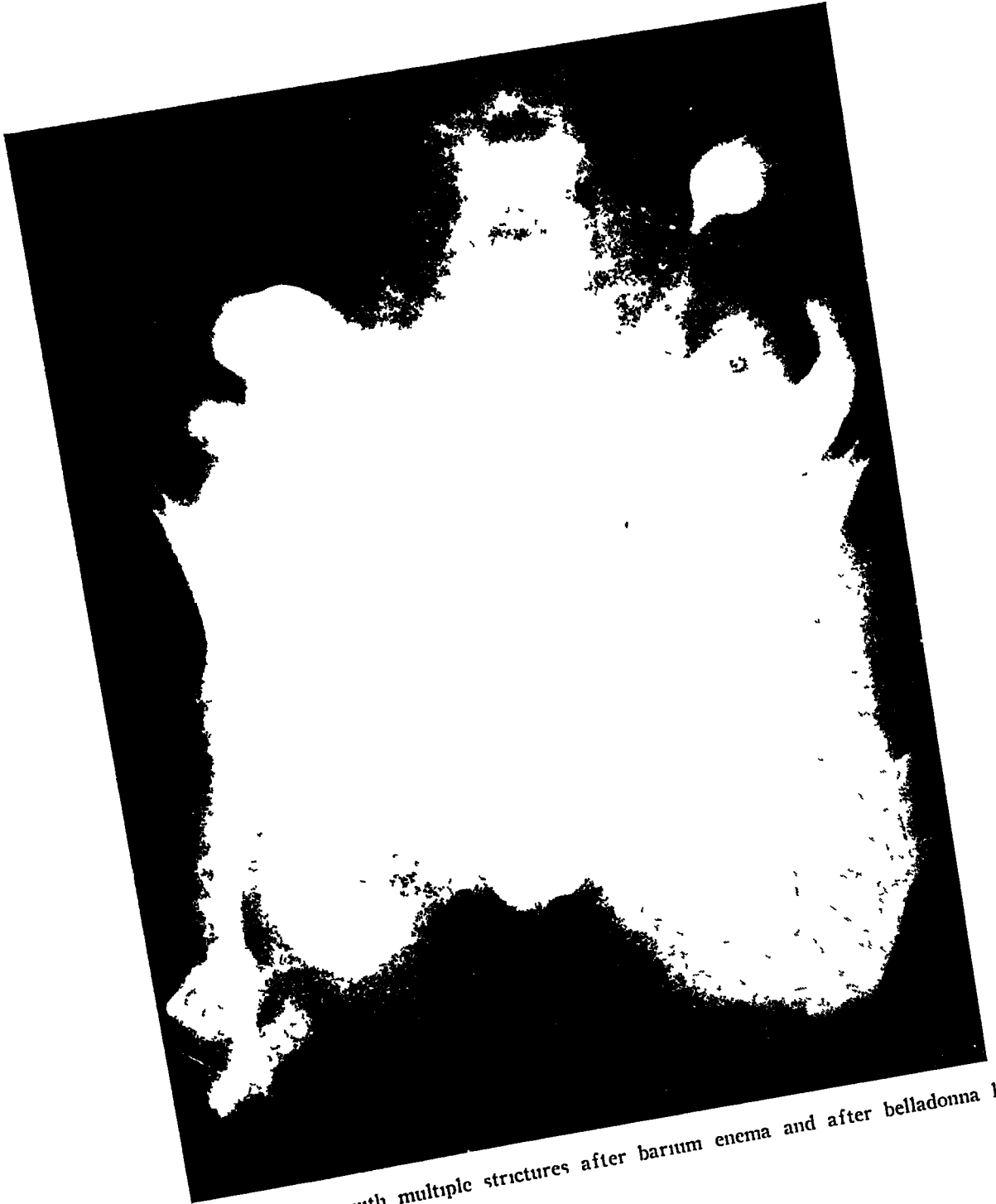


Fig 2 Colon with multiple strictures after barium enema and after belladonna had been administered





Fig 3 Multiple per rectal abscesses that had ruptured or had been incised, causing severe rectal deformity in a case of chronic ulcerative colitis



Fig 4 Colon with multiple perforations and chronic ulcerative colitis

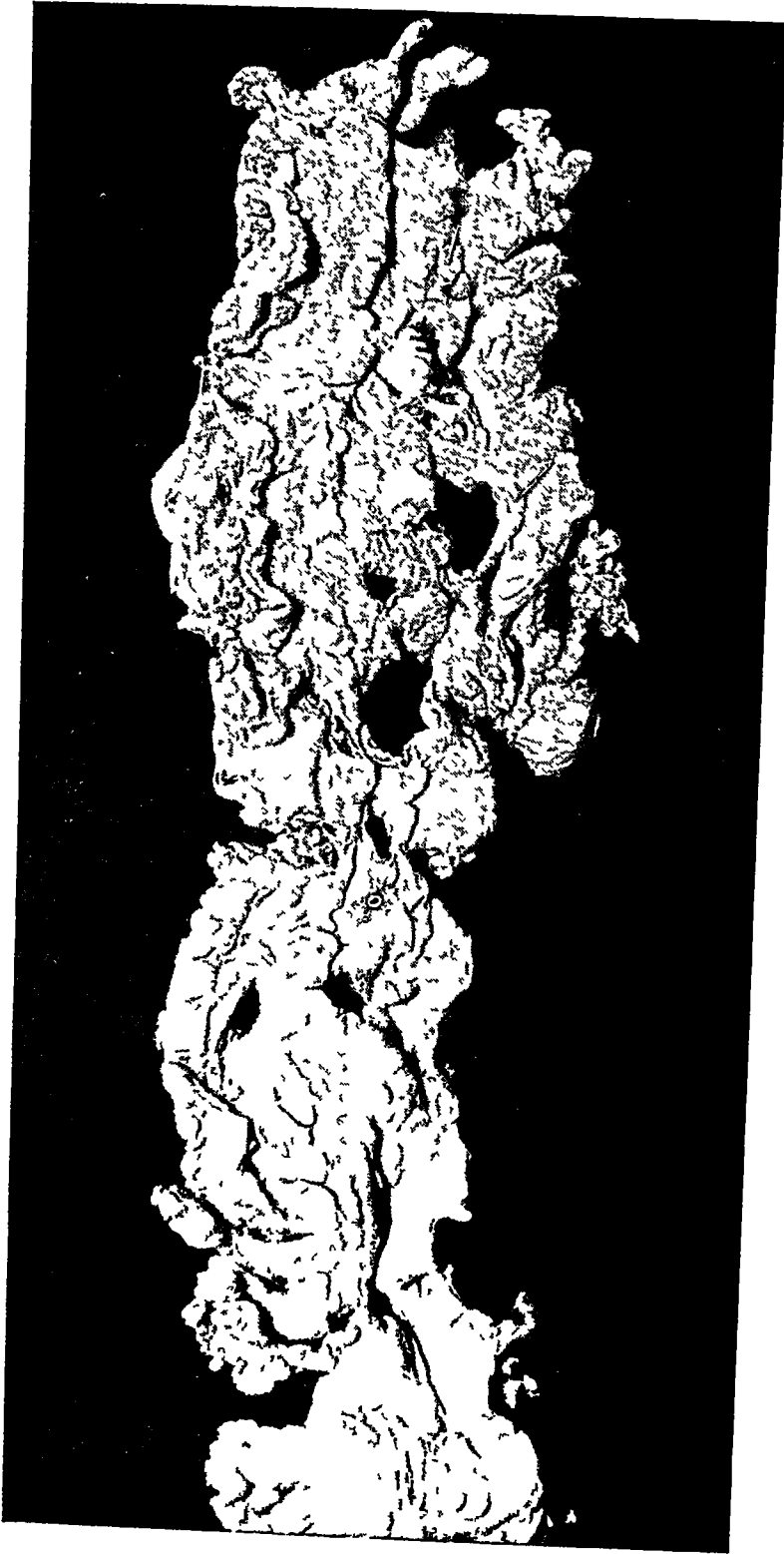


Fig 5 Part of the colon shown in figure 4

regular ulcers of the leg pityriasis rosca, neurodermatitis, erysipelas, pellagra and pemphigus. There may not be any close relationship between the colitis and most of these, but an interesting clinical observation is the fact that with relief from the colitis, a goodly number of them clear up. The repeated concurrence of erythema nodosum, arthritis and colitis is worthy of comment.

Malignant disease as reported previously<sup>1</sup> is usually of rapid, early fatal type, frequently occurring as multiple carcinoma of a high grade of malignancy in the colons of young persons and in association with polyposis.

Renal insufficiency as a complication of severe dysfunction of the colon is serious. Demonstrable renal injury has occurred only rarely in this series of cases of chronic ulcerative colitis. Evidence of such impairment has included albuminuria, hematuria, edema, increased blood urea, and elevation of blood pressure, as well as changes in the ocular fundi.

Endocarditis occurred rarely with or as a sequel to chronic ulcerative colitis. It appeared in only 1 per cent of the cases, and only once could the fatal termination of the disease be attributed to this condition. Growth was not obtained on blood culture, nevertheless, in a few other cases, in which endocarditis was not a factor, but in which chronic ulcerative colitis was severe, the diplostreptococcus of chronic ulcerative colitis was isolated by blood culture.

In seven of the 693 cases there was unusual splenomegaly. Several of these patients had enormous spleens. All but one occurred in young persons;

the ages of the patients were fifty-one, forty-two, thirty, twenty-three, twenty, fifteen and seven years. In the patient aged fifty-one years Banti's disease and biliary cirrhosis were diagnosed; in all the others, infectious splenomegaly was considered. In the case of the boy aged fifteen years, there was associated juvenile hepatic cirrhosis, so diagnosed at necropsy, and in two cases there was associated purpura hemorrhagica.

Ocular disease, although it occurred in only five cases in this series, was definitely a complication, usually in the form of iritis or uveitis. In all cases it occurred in the presence of one or more other complications; that is, perirectal abscess, endocarditis, arthritis, and erythema nodosum. This adds evidence to the theory of the blood-borne nature of these infections. Crohn<sup>5</sup> has reported several similar cases.

That fatal hemorrhage from the colon does not occur more frequently is rather astonishing when the extensively ulcerated surface present in these cases is considered.

Renal calculi are mentioned here because clinical symptoms of their presence occurred during the course of the disease.

Mesenteric thrombosis played a part in the fatal outcome in one case.

Tetany occurred in only one case in which colectomy was performed and in which there were multiple operations on the ileum for obstruction. The rarity of this symptom is striking when the terrific intractable diarrhea with which so many of these patients are afflicted is considered.

In addition to these closely associated pathologic lesions, other condi-

tions which occur in the course of chronic ulcerative colitis should be mentioned. A peculiar mental attitude develops in many cases and in twenty-five of this series there were symptoms of neurologic phenomena. Seventeen patients failed to respond to treatment and the colitis progressed toward its terminal events. Twelve other patients had duodenal ulcer, ten had ulceration involving parts of the colon, producing conditions that simulated filling defects; there were five cases of pregnancy during the course of the disease in which symptoms improved or completely disappeared during the pregnancy; in four cases lymphosarcoma occurred in the colon, there were two cases of lymphatic leukemia, and one case of pericolic lipomatosis.

It should also be noted that there were four cases in which various types of abdominal surgical procedures precipitated acute attacks of ulcerative colitis which proved fatal to the patients.

There were only five instances in which the disease occurred in more than one member of a family. Those affected in groups were two sisters, two brothers, a father and his daughter, and in two instances a mother and her son. Such an incidence could occur readily in any infection and would argue against the idea that the disease might be contagious.

#### REPORT OF CASES

*Case 1, polyposis*—A man aged twenty, was admitted to The Mayo Clinic September 26, 1925, with a history of bloody dysentery of nineteen months' duration and with a maximum of thirty to forty stools in twenty-four hours. He stated that his condition had been as bad as this for at least 100 days in succession. A diagnosis

of amebic dysentery had been made elsewhere, although amebae had not been found in the stools.

The patient was acutely ill with a maximal temperature of 102°, and he had many rectal discharges containing pus and blood. He suffered from incontinence of the rectum and had lost 24 pounds in weight. The pulse rate was 90 and the blood pressure 120 systolic and 90 diastolic. The abdomen was moderately tender. At proctoscopic examination, September 28, 1925, there were noted a diffuse granular involvement of the rectal and sigmoidal mucosa, associated edema, a hemorrhagic tendency, and scattered punched-out ulcers. The diagnosis was chronic ulcerative colitis. During the next five months his condition varied. Improvement was slow but by October 24, 1925, his condition had progressed so that he was dismissed.

The patient returned in February, 1926, much worse than on first admission, reporting steady failure during the month. On the report of proctoscopic examination made February 23, it was noted that there were large, sloughing, ragged, undermining ulcers of the rectum with bridging of the mucosa between large ulcers, a very serious condition. Ileostomy as an emergency was suggested, but because of the severity of the condition the idea was abandoned. Treatment then consisted of tincture of iodine given by mouth, large doses of kaolin alternating with bismuth, opium and paregoric, and small doses of vaccine prepared from the diplostreptococcus which was isolated practically in pure culture from the ulcers in the rectum on both occasions. He slowly began to improve and after several months was able to go home.

September 22, 1926, the patient stated that he had gained 37 pounds in weight in the preceding four months, he was having six to seven movements of the bowel in twenty-four hours with only occasionally a little blood and mucus. The proctologist reported the mucosa practically normal. There were a few pitted scars scattered over a slightly pale mucosa and multiple polyps from 0.3 to 0.7 mm wide and from 0.3 to 1.5 cm long, some bled easily. The

diagnosis was polyposis following healing of extremely advanced chronic ulcerative colitis. Clinically the patient was in excellent condition. He was dismissed with instructions to take vaccine subcutaneously. May 23, 1927, he returned, clinically well, stating that he had had the best winter since the beginning of the illness. He had gained 50 pounds in weight and looked the picture of health. There had been an average of three bowel movements daily for months and blood had not been seen in the stools for at least a month. At this time the proctologist reported healed chronic ulcerative colitis, leaving polypoid areas and polyps. Some small polyps seen January 23, 1927, had disappeared. The mucosa between polyps was normal except for the scars of the infection. A series of fulgurations of the rectal polyps was carried out without incident. The patient was free of symptoms then, but because of the inability to fulgurate all the polyps he returned in December, 1927. At this time it was noted on proctoscopic examination that there were still several polyps in the rectum but that the mucosa was healthy. The remaining polyps were fulgurated.

August 9, 1928, the proctologist noted some scars in the rectum but no ulceration. The lumen was practically normal in diameter. The areas fulgurated did not show polyps.

*Case 2, stricture*—A man aged thirty-three years came to the clinic in December, 1928, with a history of bloody dysentery of ten years' duration, accompanied by ten to fifteen bowel movements daily.

The patient was emaciated and in the last few months prior to coming to the clinic he had lost 19 pounds. Proctoscopic examination revealed chronic ulcerative colitis, a definite annular stricture 13 mm in diameter situated 2 cm above the pectinate line, and the whole rectum contracted to two-thirds its normal size. The roentgenogram showed involvement of the entire colon. The Wassermann reaction on the blood was negative. Stool examination was negative for acid-fast bacilli, parasites, and ova. Analysis of gastric content gave a total quantity of 110 cc, total acidity of 40 and free

hydrochloric acid of 18. The blood count was essentially normal, except that leukocytes numbered 10,800 in each cubic millimeter. The tonsils were septic and there was periapical infection of one tooth, these foci were removed and vaccine was given subcutaneously.

The patient returned in March, 1928, averaging three to five bowel movements daily and feeling well. At this time the proctoscope revealed activity, graded 1 on a basis of 1 to 4, with contraction of the rectum to about half its normal diameter, and the stricture admitting a large proctoscope. The patient had performed his usual business duties in the previous six months, was on the road all the time and drove his car most of the time.

*Case 3, arthritis*—A man aged forty-six years came to the clinic in October, 1925, complaining of pains in the joints of one and a half years' duration. There was a history of bloody rectal discharges for three weeks. Pains in the joints of both feet had begun a year and a half before admission. Six months later some infected teeth had been extracted and the pain had left the joints but had returned four weeks later. Then it had shifted to the neck, right shoulder, arm and wrist. At the time of admission it involved one wrist and the knees. Tonsillectomy had been performed without relief, three months previously.

On admission the patient's temperature was 99.2° at 8:30 a. m. and the pulse rate was 100. He had some definite stiffness of the neck and back. The right wrist was swollen and numerous joints were stiff. October 10, 1925, the hemoglobin was 75 per cent, erythrocytes numbered 4,760,000 and leukocytes 8,700 in each cubic millimeter. The Wassermann reaction on the blood was negative. Roentgen-ray examinations of the teeth, neck, wrist, knees, chest and colon gave negative results. The proctoscopic examination revealed chronic ulcerative colitis for 24 cm, graded 2+. He was given prostatic massage because of non-specific prostatitis, graded 3.

During a period of observation for twenty days after admission the bowel movements were ten to twelve in twenty-four hours,

all mixed with blood. In the third week of his stay the patient received a vaccine filtrate made from the diplococcus which was isolated from the lesions in the rectum. Improvement was marked and two months after admission the bowel movements were reduced to one or two in twenty-four hours. For the arthritis he was given baking and massage. He was dismissed December 16. The bowel apparently was in excellent condition, the arthritis had not improved.

The patient returned home, the arthritis improved progressively and he returned to work. In April, 1926, arthritis returned and for a month he was partially incapacitated because of swollen and sore joints. About the middle of June iritis developed, first in the left eye and then in the right. Four days after the onset he had an acute exacerbation of bowel trouble with ten to fifteen stools in twenty-four hours, the stools contained blood, pus and mucus and there was much cramping, tenesmus and extreme soreness in the lower part of the abdomen. This continued until he returned August 10, 1926.

A roentgenogram at this time showed chronic ulcerative colitis of the left half of the colon. Hemoglobin was 64 per cent, erythrocytes numbered 4,270,000 and leukocytes 5,600 in each cubic millimeter of blood. Of the leukocytes, 53 per cent were polymorphonuclear neutrophils. Parasites or ova were not found in the stools and smears from the rectal ulcers did not contain acid-fast bacilli. Treatment with vaccine filtrate administered subcutaneously and with baking and massage was resumed August 16 and by September 24 the bowel movements were reduced to two stools daily, the patient had gained 17 pounds in weight, the rheumatism had improved and from every standpoint he was better. He was dismissed and continued to take vaccine at home for the chronic ulcerative colitis. He stated that as long as he took the vaccine he remained well.

In the first part of January, 1927, trouble returned with ten to twelve blood-streaked stools, and coincident with the recurrence of colitis was an acute flare-up of arthritis. The patient wrote for more vaccine and

after taking it a month said that all his symptoms again had subsided. However, a month before his return on April 11, 1927, symptoms recurred. On admission he made the statement that when he did not have colitis, he did not have arthritis, and that with an upset of the bowels, the arthritis recurred. The treatment formerly given was resumed and two weeks after its institution he again was dismissed very much improved, he was passing only two stools a day and the symptoms of arthritis were very mild.

The next admission was June 13, 1928. At this time the colitis had recurred with twelve to fifteen bloody stools a day but without an exacerbation of arthritis. During the patient's last period in the hospital he was given the concentrated chronic ulcerative colitis serum, described elsewhere,<sup>2</sup> and since his dismissal, August 24, 1928, he has improved steadily.

The interesting point in this case is the apparent close relation between the arthritis and the colitis, without any other apparent or demonstrable focus.

*Case 4, perirectal abscess*—A man aged fifty-eight years came to the clinic May 27, 1927, with a history of bloody diarrhea of one year's duration. He had been in hospital elsewhere for five weeks and stated that daily examinations of the stool had not revealed parasites or ova. In spite of this he was given intensive treatment for amebic infection.

On admission he was having about one stool every hour of the twenty-four, with blood, mucus and pus. His weight was 152 pounds. Hemoglobin was 64 per cent, erythrocytes numbered 3,860,000 and leukocytes 7,800 in a cubic millimeter of blood. Of the leukocytes 80 per cent were polymorphonuclear neutrophils. The Wassermann reaction on the blood was negative. Three examinations of the stool were negative for parasites, ova and acid-fast bacilli. The tonsils were infected and two dental roots had periapical infection. The proctoscopic examination revealed chronic ulcerative colitis, graded about 2. The diplostreptococcus of chronic ulcerative colitis was isolated from the rectal ulcers and the pa-

tient was given vaccine subcutaneously. By June 18, he had made definite improvement, he had gained some weight, and stools had been reduced to nine in twenty-four hours. He was dismissed and was advised to continue the vaccine. His improvement was steady until the middle of November, 1927. During his stay at home two abscessed teeth were removed. Nine days before readmission December 20 he had pain around the anus, due to what he thought was a boil on one side of the rectum. This was lanced before his return to the clinic and at least 180 cc of pus was drained from it. Thereafter the perirectal pain had been very severe. On admission he had an acute exacerbation of chronic ulcerative colitis with a huge, severe perirectal abscess. The temperature was 102.5°. The hemoglobin was 58 per cent, erythrocytes numbered 3,360,000 and leukocytes 12,100 in each cubic millimeter of blood. Sixty per cent of the leukocytes were polymorphonuclear neutrophils. Continuous hot dressings were applied to the rectum. December 22, a large perirectal abscess was drained and the culture obtained revealed the diplostreptococcus of chronic ulcerative colitis. From this a fresh vaccine was prepared. Following the drainage a fistulous tract developed through the abscess into the rectum. By January 14, inflammation had subsided and bowel movements had been reduced from a maximum of eighteen in twenty-four hours to six. Again he was dismissed. Improvement was steady. He returned for reexamination September 4, at which time the proctoscope revealed the mucosa still granular, the sinus tract had practically healed. January 3, 1927, tonsillectomy was done without incident. His weight at this time was 167 pounds and he was averaging three to four daily bowel movements and he felt well.

*Case 5, nephritis and nephrosis*—A man, aged thirty-two years came to the clinic April 12, 1928, with a history of bloody dysentery of ten years' duration. His trouble had begun with bloody bowel movements and severe abdominal cramps after six months' service in the United States Navy. During the first three or four months of his trouble his weight had fallen from

140 to 90 pounds. He was not sure of the exact number of bowel movements but frequently they were as often as once an hour, day and night. Appendicostomy had been done—after he had been sick about six months and irrigations of ichthyol were given through the appendicostomy opening. In three or four months he had been free of symptoms. A year later his trouble had recurred in a way similar to the former onset. It had been mild then until the summer of 1921 when the bloody diarrhea had become worse. Cecostomy had been done but improvement had not followed and the cecostomy opening had been closed. A year later colostomy had been done but the opening had been closed fifteen months later. Progress had not been satisfactory, therefore colostomy had been done a second time. In January, 1927, a course of medication had been begun, but improvement had not resulted.

The patient's symptoms continued and on admission to the clinic April 12, 1928, he gave a history of progressive increasing bloody discharges for which he had had ten major surgical procedures. He presented himself with a malfunctioning cecostomy opening and much dehydration, continuous vomiting and symptoms of intestinal obstruction. After intravenous administration of glucose and withholding of food by mouth, his condition improved markedly. The obstruction relieved itself and his progress was such that examinations concerning the nature of the disease could be instituted. At this time albuminuria was graded 3, hyaline casts 2, granular casts 3, and pus 1. The blood urea was 114 mg for each 100 cc, the blood chlorides, 543. Hemoglobin was 46 per cent, erythrocytes numbered 3,030,000 and leukocytes 6,700 in each cubic millimeter of blood. Of the leukocytes 49 per cent were polymorphonuclear neutrophils. Systolic blood pressure was 140, the diastolic 80. In the ensuing fifteen days, progress was very satisfactory. The blood urea was reduced to 33 mg for each 100 cc, and the weight rose from 117 to 129 pounds as diet was increased. The combined phenolsulphonephthalein test of renal function gave a 15 per cent return of the



occasional trace of blood. He was gaining weight. A report in November stated that he had returned to work.

*Case 6, endocarditis*—A man aged fifty years came to the clinic January 24, 1925, with a history of severe bloody diarrhea of four months' duration. It was found that in his early childhood he had had attacks of diarrhea that had come on about every six months. During this time he would have three to seven stools daily.

At the time of proctoscopic examination chronic ulcerative colitis was noted. By roentgenogram this was found to involve the entire colon. Roentgenograms of the stomach and chest were negative. Hemoglobin was 68 per cent, erythrocytes numbered 3,610,000 and leukocytes 8,100 in each cubic millimeter of blood. The blood urea on two examinations was, respectively, 20 and 14 mg. The Wassermann reaction on the blood was negative. The blood pressure was 86 systolic and the diastolic pressure was not satisfactorily obtainable. The course of the patient while in the hospital was progressively downward and he died, February 14, 1925.

Postmortem examination revealed (1) chronic ulcerative colitis, (2) chronic mitral endocarditis with an acute exacerbation, and (3) infarcts in both kidneys.

*Case 7, splenomegaly*—A boy aged fifteen years came to the clinic in June, 1928, with a history of bloody dysentery of four years' duration. He had passed about twelve stools daily, some days he would have as many as fifteen. Two years previous to his coming to the clinic, his home physician had found that he had had a large liver.

The patient was anemic, and appeared slightly yellow. His usual weight of 117 pounds was reduced to 102 pounds. Systolic blood pressure was 114 and diastolic 82. The pulse rate was 82 and the temperature 99.2° in the afternoon. In the upper left portion of the abdomen a large, movable, firm mass, thought to be the spleen, was palpable. The hemoglobin was 40 per cent, erythrocytes numbered 3,390,000, and leukocytes 7,200 in each cubic millimeter. Of the leukocytes 69.5 per cent were polymorphonuclear.

dye injected April 13, 18 and 25, respectively. Repeated examinations of stools revealed large amounts of pus and blood but no parasites or ova. Seven urinalyses in twelve days gave essentially the same results as those noted on admission except that in some of the specimens there was a slight reduction in the number of casts and erythrocytes. With the proctoscope, it was seen April 14 that the bowel was contracted to about a third of its normal diameter and that there was much scarring and that bleeding was induced with slight trauma. A diagnosis of chronic ulcerative colitis, grade 2, was made. The roentgenogram showed involvement of the entire colon, with very marked contraction and narrowing, and at many places the lumen was only a few millimeters in diameter. Vaccine was given subcutaneously for two months. The patient's condition improved markedly and there was marked lessening of the rectal discharges. Examination of the blood June 11 revealed hemoglobin of 67 per cent, erythrocytes numbered 4,320,000 and leukocytes 8,500 in each cubic millimeter of blood. Because of the recurrent attacks of obstruction at the site of the cecostomy and because it seemed hardly possible that the colon ever would assume a useful function, ileostomy was done, June 19, 1928. The postoperative course for the first seven-teen days was uneventful. At this time the output of urine decreased and repeated examinations of the urine showed albuminuria graded 4, hyaline casts 4, granular casts 3, erythrocytes between 1 and 2 and pus between 1 and 2. Blood urea July 13, the day it was at its maximum, was 181 mg for each 100 cc. The chlorides were reduced to 417 and the carbon dioxide combining power to 46 volumes per cent. Clucose was administered and by July 28 the blood urea had dropped to 82 mg. Progress of the patient after that was continuous, and by August 22, the time of dismissal, the blood urea had been reduced to 43 mg for each 100 cc, and creatinine to 3 mg. The patient's general condition seemed good. He was on a limited intake of fluid. His bowels seemed to be in good condition, there was very little discharge and only an

blood urea was 28 mg in each 100 c c It seemed obvious that there were two conditions to treat, an acute perirectal abscess and severe chronic ulcerative colitis Local application of heat to the rectum and deep injection of the concentrated serum into the muscles were begun The abscess opened spontaneously on the third day of his stay in the hospital and following this, there was much drainage of purulent material from the rectum and the abscess cavity Examinations of the stools and drainage material for parasites and acid-fast bacilli were negative but culture of each yielded the usual diplostreptococcus found in patients with chronic ulcerative colitis

Three weeks after admission acute redness and swelling of the left eye developed In consultation with the ophthalmologist a diagnosis of marginal keratitis and acute iritis was made Treatment of this was instituted at once The patient recalled at this time that he had had a similar condition with the former upset of the bowels in 1922 Because of the acute condition of the bowels, it did not seem advisable to make a roentgenogram of the colon until December 1 When made, however, it showed subacute ulcerative colitis of the entire colon The patient's progress was slow but progressive Fifty-two days after admission he was dismissed, the abscess was practically healed and two to four formed stools without blood were being passed daily He was advised to return for observation in about six months

*Case 9, fatal hemorrhage*—A man aged thirty-nine years came to the clinic, January 19, 1922, complaining of intermittent diarrhea which had persisted over a period of twenty-five years He had been at The Mayo Clinic in 1902, at which time he had been given some medicine which had not relieved him He was having between three and five fluid, light-colored, frothy and blood-streaked stools a day Since 1900, he had been confined to bed for from two to six weeks with each of three severe attacks of diarrhea, during these attacks he became weak, emaciated, and could not work for months afterward In the last few years he had become worse and he had had difficulty in controlling the bowels

There had been much tenesmus, backache, and pain in the rectum Herpes labialis with sores inside the mouth often had accompanied the attacks He did not remember having had fever, chills or sweats There had been much accumulation of gas and occasional emesis

The patient was fairly well nourished and weighed 138 pounds The systolic blood pressure was 100, and the diastolic 60 The temperature was 98.4° at 9 30 a m There was slight tenderness of the lower portion of the abdomen and the sphincter ani was practically functionless At this time total gastric acids were 70 and free hydrochloric acid was 50 The hemoglobin was 60 per cent, leukocytes numbered 8,300 and erythrocytes 3,710,000 in each cubic millimeter The roentgenogram showed that chronic ulcerative colitis involved the entire colon The roentgenogram of the chest was negative Proctoscopic examination revealed chronic ulcerative colitis and rectal stricture, the latter was about 4 cm above the anus and was 1 to 2 cm wide

Treatment consisted of irrigations with hot physiologic solution of sodium chloride, instillations of olive oil and bismuth, a rather generous diet, oxyquinolin sulphate (chinosol), instillations of witch hazel and benetol, and emetin hypodermically

The patient was dismissed February 20, 1922, somewhat improved, and returned two years later, at which time he said the diarrhea had continued without much change, the bowel movements varying between six and twelve in twenty-four hours He complained again about stabbing pains at the costal margin posteriorly These had become much more severe since he had been in the clinic last and they continued for an hour or so at a time The pains would come on suddenly, reached their maximum in thirty minutes, continued steadily and intensely and were so severe that he would roll on the floor with pain His family and his physician said he was jaundiced after one of these attacks

At examination hemoglobin was 25 per cent; erythrocytes numbered 2,300,000 and leukocytes 6,300 in each cubic millimeter Polymorphonuclear neutrophils were 64 per cent Coagulation time was ten minutes

and bleeding time one minute. The patient belonged to blood group 4. Calcium coagulation time was nine minutes. The Wassermann reaction on the blood was negative. The tonsils were infected. The roentgenogram of the colon revealed chronic ulcerative colitis and stricture of the sigmoid. February 27 and March 4 and 11, respectively, he was given three blood transfusions and March 17 a permanent ileostomy of the modified Brown type was made. Postoperative progress was not satisfactory. There was a gradual rise in fever, increased weakness and a feeling of exhaustion. He died March 22, 1924, at which time the colon was filled with blood (2,000 cc) and there was also terminal peritonitis.

*Case 10, renal calculi.*—A woman aged nineteen came to the clinic in October, 1920, with a history of bloody dysentery of three years' duration. The first attack lasted five months with a maximum of twelve stools in twenty-four hours. She had a remission of about one month after which the trouble recurred. Her condition was worse during the winter. Increase in the number of stools and cramps often occurred during the night. She passed blood, mucus, pus and loose stools even when she was at her best, and during the three years the smallest number of stools had been three to four a day. During the winter previous to admission she had had much trouble with arthritis, the joints affected included ankles, elbows and knees, which had been swollen, stiff and very tender. At this time she had first had spells of pain in the right loin, so severe that her face would be drawn and she would talk incoherently. These attacks would last one to two hours.

On admission she was having about twelve stools in twenty-four hours. She was thin, emaciated, anemic and had lost 35 pounds in weight in the three years. The hemoglobin was 36 per cent, erythrocytes numbered 3,850,000 and leukocytes 17,600 in each cubic millimeter. Except for a trace of albumin, a few erythrocytes and 10 to 25 pus cells in each high powered field, urinalysis was negative. Parasites, ova or acid-fast bacilli were not found in the stools on repeated examination. Proctoscopic examination revealed chronic ulcerative colitis

with the lumen of the bowel reduced to a fifth the usual dimension, and marked activity of the process. Because of the marked narrowing of the bowel and the history of continued trouble, ileostomy of the modified Brown type was done November 3, 1920. The postoperative course was uneventful and the patient got along well with the ileostomy opening. She returned to the clinic in November, 1925, she had gained 10 pounds in weight, in general felt well and hoped that she might have the ileostomy opening closed. She said, that a year after leaving the clinic she had had an acute flare-up of arthritis and that most of the joints had been involved. There had been frequent flare-ups of the colonic condition, with blood, mucus, and pus discharging from the rectum. There had not been any more attacks of the severe pain in the right side, but there had been spells of frequency and burning on urination without hematuria.

In four examinations of urine on as many days albuminuria was graded 3, erythrocytes 3, and pus 4. Two of these specimens were obtained by catheterization. Test of renal function gave a return of 40 per cent of the dye injected. Several urinalyses were negative for acid fast bacilli. Infected tonsils were removed September 7. Roentgenograms of the kidneys showed the presence of huge, bilateral renal stones. At this time it was noted also that the patient had papular cutaneous lesions of the extremities and hips. These had appeared in three attacks with exacerbations of the colitis. The lesions were papulonecrotic tuberculids.

In summary, then, the patient had extensive, chronic ulcerative colitis with rectal stricture, arthritis, bilateral renal stones and papulonecrotic tuberculids. Her general condition seemed fairly good, and the treatment consisted of a series of injections of neo-arsphenamine, vaccine subcutaneously, and symptomatic relief of the symptoms referable to the bladder. The last report from her, in 1928, showed that her condition had continued about the same.

*Case 11, mesenteric thrombosis.*—A girl aged fifteen years came to the clinic early in February, 1923, with a history of dysentery of one and a half years' duration

The trouble had started after a camping trip and she had suffered from what seemed to be ordinary "summer complaint," but the condition had continued. There had been six daily stools with mucus, but without blood and pain. There had been a gradual increase in the trouble until she had had eight to nine stools a day containing mucus and blood. Reclining had not affected the frequency of the stools. Various medicines used had given slight, if any, temporary relief. Diet did not have any appreciable effect on the symptoms. She had lost about 6 pounds in weight and on admission weighed 99 pounds.

The blood count was essentially normal except that leukocytes numbered 10,000 in each cubic millimeter. A roentgenogram of the chest was negative and that of the colon showed the deformity of chronic ulcerative colitis. Repeated examinations of the stools were negative for parasites, ova and acid-fast bacilli. The proctoscopic examination revealed chronic ulcerative colitis with an activity of 3 on a basis of 4. A special examination of the heart was made. Medical management with local irrigations and tincture of iodine by mouth did not give apparent relief, in fact the patient seemed to be worse at the end of a month's treatment. Appendicostomy was done March 5, 1923, and about two-thirds of the appendix was removed. The patient's postoperative progress was only fair at first and later there was progressive failure. She died April 19, 1923.

The postmortem diagnosis was chronic ulcerative colitis of the entire colon, with anemia and acute enteritis of the terminal

ileum, emaciation, graded 3, and extensive intra-abdominal venous thrombosis.

### DISCUSSION

Chronic ulcerative colitis is a serious infection of the colon. Its early diagnosis is imperative. This means careful examination of stools for parasites and unusual bacteria, observation of the stools for blood, mucus, and pus, careful consideration of the time of passage of stools and the conditions of tenesmus, urgency, and pain with evacuation of the bowels. Passage of blood, mucus and pus by rectum is unnatural. Careful inquiry into conditions which existed early in the period over which blood, mucus and pus were observed in the stool usually gives definite and important diagnostic data.

Proctoscopic examination should be employed in all cases of diarrhea, of discharge of blood, mucus, or pus by rectum, or of any rectal bleeding.

A roentgenogram of the colon after barium enema is the next most valuable diagnostic aid.

Finally, the importance of taking a careful history in all cases suggesting colonic disease stands out as the most important diagnostic aid.

With early diagnosis early treatment can be instituted and many of the serious complications can be avoided.

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# Atypical Clinical Forms of Trichiniasis\*†

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**T**RICHINIASIS in this country is far from being a rare disease, yet it seems not to have established itself in the mind of the average practitioner as one of those diseases to be thought of and watched for. For this attitude there are doubtless many reasons, but one of these seems to be the fact that there still exists the feeling, carried over from the early writings upon the subject, that trichiniasis occurs usually in the form of epidemics; whereas in point of fact most of the cases met with occur either as sporadic isolated examples or in groups of only two or three.

Another of the reasons for the common failure to recognize the disease lies in the fact that trichiniasis presents a clinical picture of much greater variability than is the case of most specific infectious diseases.

It is the purpose of this discussion to call attention to some of the many variations from the conventional and readily recognizable clinical picture. These variations have long been known and are referred to in most text book articles on the subject, notably in the

admirable review of the subject by George Blumer,<sup>1</sup> but they seem sufficiently important to justify their further consideration.

During the past 15 years there have been treated in the medical wards of the New York Hospital 52 patients in whom the diagnosis of trichiniasis was made.\* It is interesting to note that 47 of these cases occurred as isolated instances of the disease and that no history of others having been infected could be obtained. Of the remaining five patients three were members of one family and two were young women who lived together. Among such sporadic cases the graver types of the disease seem much rarer than is usually the case in the larger epidemics. No deaths occurred among the 52 patients referred to.

Before discussing the atypical clinical forms of trichiniasis it will be necessary to review briefly the usual clinical picture.

The resemblance of the average case to that of a mild or moderately severe case of typhoid fever has often been pointed out. There is usually a fairly abrupt onset, with fever, headache and malaise, and either with or without gastro-intestinal symptoms. The febrile period may last from a week or ten days to several weeks, the fever usually ranging fairly high and falling

\*With the kind permission of my colleague Dr W R Williams I have included with my own those cases that have occurred upon his service.

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by lysis. The prominence of muscular pain and soreness as a symptom varies greatly. Such pain and stiffness may be conspicuous and protracted, may be widely distributed or limited to special groups of muscles, or may be almost entirely wanting. Subcutaneous edema is a common and important early symptom that is usually fleeting and is often only recognizable about the eyelids and face. It is by no means always present however even in the early days. Cough, sweating and injection of the conjunctivae are among the common symptoms. The spleen ordinarily is not palpable. One of the most important diagnostic features of the disease is the early and marked increase in the eosinophile leukocytes, associated usually with some degree of leukocytosis.

With this brief description of the usual, conventional clinical picture we may now turn to a consideration of the unusual clinical types.

#### ATYPICAL CLINICAL FORMS

In general it may be said that no one of the above-named symptoms is essential or constantly present, and that any one or several of them may be lacking, or at least may be so inconspicuous as to pass unnoticed.

*Cases Without Fever*—Although fever of some degree is perhaps the most constant of all the symptoms the almost complete absence of fever is seen in two types of cases, (1) those extremely mild or symptomless cases seen among the members of an infected family, which are recognizable only by the characteristic changes in the blood picture, and (2) cases with a very protracted course in which the

chief symptom is localized pain or soreness. In some of these, by careful questioning, a history of an onset with mild fever and malaise may be obtained but in other instances the diagnosis may have to rest only on the history of an initial edema of the face, the presence of the characteristic high eosinophilia and, perhaps, the demonstration of the parasites in the excised muscle.

Occasionally after an initial gastrointestinal attack there may be an interval of several weeks with little or no fever before a period of continued fever ensues.

*Cases With No, or With Only Very Late, Eosinophilia*—The constant presence of a high proportion of eosinophilic leukocytes in the blood has come to be looked upon as so essential to the diagnosis of trichiniasis that the absence of such an eosinophilia is apt to be regarded as sufficient ground for the rejection of this diagnosis. In general such an attitude is justified, but it must be emphasized that this rule of a high eosinophilia is by no means absolute. Bartlett<sup>2</sup> records an interesting case, fatal after seven weeks of illness, in which, although there was a leukocytosis of from 19,000 to 20,000, the eosinophiles did not rise above one per cent. The diagnosis was confirmed by autopsy and a histological study of the inflamed muscle showed round-celled infiltration composed of polymorphonuclear neutrophils and small mononuclears, with only an occasional eosinophile cell. Similar fatal cases without eosinophilia are reported by Howard<sup>3</sup> and by Maase and Zondek.<sup>4</sup> Such an absence of eosinophilia throughout the

entire course of the disease seems however to be very rare. Of more frequent occurrence is the failure of the eosinophiles to appear until several weeks after the onset of the illness.

Gregg<sup>5</sup> cites the case of a boy of 11 years, severely ill and suspected of having typhoid fever, who showed no eosinophile cells until more than three weeks after the onset. Several days before the appearance of an eosinophilia a piece of excised muscle had shown the presence of many of the parasites. Cabot<sup>6</sup> refers to a case in which there was absence of eosinophilia during the first ten days of illness.

A woman on the service of my colleague, Dr W R Williams, ran a febrile course, with edema of the face and legs, for six weeks before the advent of an eosinophilia. Several days before this occurred the excised muscle had revealed the presence of trichinellae.

*Case I*—Among my own cases is that of an Italian boy of 11 years who, after an illness of three weeks, was referred to the hospital with the diagnosis of acute nephritis. He had had continuous slight fever, vomiting, lumbar pain and profuse sweating, as well as a marked subcutaneous edema which at the time of admission to the hospital was especially pronounced about the face and eyes. The urine however showed only a trace of albumin and a rare granular cast and various renal function tests yielded fairly normal results. In spite of the fact that the blood showed no eosinophiles whatever it seemed probable that the case was one of trichiniasis and frequent blood examinations were

made. Five days after admission, among 7,200 white cells, there were three per cent of eosinophiles. This count remained unchanged until nine days later (i.e. five weeks after the onset) when the percentage of eosinophiles suddenly rose to 28. By that time most of the symptoms were subsiding. Ultimately the eosinophiles reached 36 per cent of a total leukocyte count of 16,000. A biopsy revealed many encysted larvae.

From the instances cited above it is clear therefor that even so characteristic and constant a symptom as eosinophilia may occasionally be lacking entirely or may appear only several weeks after the onset of the acute symptoms.

*Cases Showing a Positive Widal Reaction*—The close resemblance of the clinical picture of many cases of trichiniasis to that of typhoid fever has already been referred to. This resemblance is usually confined to the general course of the fever and to the associated constitutional symptoms. Occasionally the similarity is made closer by the presence of a splenic tumor and of a scanty eruption over the trunk which bears some resemblance to the rose-spots of typhoid fever. In rare instances however the resemblance becomes even more confusing because of the presence of a positive Widal reaction.

*Case II*—A man, aged 42 years, was admitted to the First Medical Division of the New York Hospital after six weeks of illness beginning abruptly with headache, nausea and dizziness. This onset was followed by a diarrhea lasting a week or ten days and by muscular pains and great weak-

ness He had noticed no swelling of the face or eyes and thought he had had no fever His temperature, on admission, was 102° and he continued to have a moderate fever for three weeks The spleen was not palpable but over the abdomen were several small pinkish spots resembling rose-spots The blood showed a leukocytosis and the eosinophile cells, which at first were only three per cent of the total, gradually increased to 43 per cent Repeated Widal tests always gave a strongly positive Widal reaction and at one time complete agglutination was obtained in a dilution of 1 to 2,560 Agglutination tests with B paratyphosus A and B, with B. coli and with B dysenteriae were all negative Many fruitless efforts were made to recover B typhosus from cultures of the blood, stools and urine, and of bile obtained from the duodenum Trichinella larvae were demonstrated in muscle obtained from the lower end of the biceps

If this case were considered alone one might be inclined to feel that, in spite of the many unsuccessful efforts to prove the existence of typhoid fever, an infection with B Typhosus must have been present along with the trichiniasis; but the case does not stand alone Maase and Zondek<sup>4</sup> have reported three typical and fatal cases of trichiniasis in each of which the Widal reaction was positive in a dilution of 1 to 400, and in each of which the autopsy proved the existence of trichiniasis and the absence of typhoid fever. They note, however, that in spite of the strongly positive reaction to the Widal test, the response to Ficker's modification of that test (with dead bacilli) was negative. None of

the patients had ever received prophylactic vaccination against typhoid

In a second case of proved trichiniasis in the New York Hospital series (from the service of Dr Williams) the first two Widal tests were negative, a third was definitely positive and a fourth, ten days later, was again negative

There can be no doubt, therefore, that for some reason quite unknown, the serum of a trichiniasis patient may occasionally cause agglutination of typhoid bacilli even in high dilutions

#### *Cases Resembling Acute Nephritis —*

In no symptom is there greater variation to be found than in that of the degree of subcutaneous edema present. Such edema may be lacking entirely or may amount to general anasarca It usually appears first, and is most pronounced, about the eyes and face

It is not surprising therefore that the rapid development of a generalized edema in an acutely ill patient should at first suggest acute nephritis Throughout the literature of trichiniasis are frequent references to cases with pronounced and generalized subcutaneous edema Cabot<sup>5</sup> speaks of a case in which there was not only general anasarca but dropsy of all the serous cavities as well Case I furnishes a good example of this clinical type, in which the true diagnosis was further obscured by the fact that no eosinophilia appeared until five weeks after the onset of the illness

#### *Cases Simulating Meningitis —*

J. Meyer reports three cases of trichiniasis, occurring in children of 6, 8 and 12 years respectively, which upon admission to the Cook County Hospital were sent to the Contagious Wards,



with the diagnosis of epidemic meningitis. In the most striking case there were delirium, marked irritability, photophobia, rigidity of the neck, a strongly positive Kernig's sign and absent knee jerks. In all of the cases, however, the spinal fluid was clear and had the characteristics of that of anterior poliomyelitis rather than of meningitis. The cells were increased to from 40-240 per c mm. In one case the trichinella larvae were recovered from the spinal fluid. In the case of Van Cott and Lintz,<sup>8</sup> in which recovery of the parasites from the spinal fluid is recorded for the first time, the patient had pronounced meningeal symptoms and a similar case is cited by McDonald and Waddell.<sup>9</sup> In the reports of several of the early writers emphasis is laid upon the frequency with which a positive Kernig sign and rigidity of the muscles of the neck are found in this disease.

*Cases with Conspicuous Throat Symptoms*—Even in the early great epidemics in Germany it was noted that throat symptoms were sometimes very pronounced and that the laryngeal and throat muscles were apt to contain great numbers of trichina larvae.

Mackenty<sup>10</sup> has reported a series of three cases, infected at the same time, in which there were alarming symptoms of laryngeal obstruction. In the most striking case, a woman 60 years old, the patient was found propped up in bed, cyanotic and struggling for breath, with inspiratory stridor and a rapid, feeble pulse. Examination showed edema of the soft palate and of the lateral pharyngeal walls, ex-

tending over the epiglottis and obscuring the parts below. In addition there were pain and stiffness of the neck, jaws, face and tongue. The onset had occurred one week before, with fever, malaise, intense headache, diarrhea, muscular pains and severe, dry cough. The edema of the glottis subsided within three or four days and the diagnosis was established by a high eosinophilia in all of the cases.

*Cases Simulating Frontal Sinusitis*—Edema about the eyes, injection of the conjunctivae and soreness and pain on movement of the eyeballs are so common as to belong among the usual symptoms of the disease, but occasionally these eye symptoms may be so prominent as to dominate the clinical picture. E. L. Pratt<sup>11</sup> has recorded three cases in each of which the patient was referred to the rhinologist because of a suspected frontal sinusitis. There was edema of both eyes, but the chief complaint was severe pain over one frontal region. The absence of definite signs of sinusitis, together with edema of the eyes and the finding of a high eosinophilia led to the correct diagnosis. Thomas and Cooper<sup>12</sup> report the somewhat similar case of a man, ill for three weeks with fever, muscular pain and soreness, who developed great edema of the eyelids and complained of such severe frontal pain as to require morphine. Orbital abscess and empyema of the sphenoidal sinus were each suspected. The diagnosis of trichiniasis was established by the eosinophilia and the results of a biopsy.

*Cases with Epigastric Pain as the Chief Symptom*—In the earlier writings on the subject of trichiniasis ref-

erences are occasionally found to cases in which epigastric pain has constituted the only symptom. The following cases from my own service are examples of this clinical type.

*Case III*—An Italian man of 38 years was admitted to the hospital with the diagnosis of peptic ulcer. He had been well up to two weeks before, when he was seized with sudden sharp epigastric pain lasting about one hour. Thereafter these attacks of severe pain recurred several times daily, coming on usually after meals and lasting from 15 minutes to one hour. He complained of no other symptoms and was well enough to continue his work as a longshoreman. He had no fever, and the physical examination revealed only some puffiness about the eyelids and some tenderness in the region of the umbilicus. A gastro-intestinal X-ray examination was negative. The leukocytes however, were greatly increased (20,000-34,000) and the percentage of eosinophiles varied between 44 and 85. A bit of muscle excised from the lower end of the biceps contained trichinella larvae.

*Case IV*—In a second case, also an Italian man, the patient two months before admission had had a sudden chill, followed by fever of two or three days duration. At the same time he developed muscular soreness all over the body which was so severe as to confine him to bed for two weeks. At the end of that time the general soreness disappeared but he began to have localized soreness, but not actual pain, in the upper abdomen, sometimes in the epigastrium and sometimes in the umbilical region. This discomfort, which had continued for six weeks,

was not constant but would come on at irregular times during the day and bore no relation to meals. He had no fever and complained of no other symptoms. The abdomen was soft and free from tenderness. Gastro-intestinal X-ray examinations were negative and the only physical sign was some puffiness about the eyes. The leukocytes were not increased in number, but there was an eosinophilia which increased from 10 to 37 per cent. Although no parasites were found in the excised muscle, the slight edema of the face and the high proportion of eosinophiles seemed to justify the diagnosis of trichiniasis.

In cases such as these just described it has been customary, rightly or wrongly, to explain the epigastric pain by the assumption of a severe invasion of the diaphragm by the migrating parasites.

#### SUMMARY

The usual clinical picture of trichiniasis is so characteristic and easily recognizable that the diagnosis in typical cases presents no difficulties, but there are many cases in which either the pathognomonic symptoms are so wanting, or the clinical picture resembles so closely that of other diseases, that mistakes in diagnosis are not easily avoided.

Some of the many possible variations from the conventional clinical type have been discussed and illustrated.

It has been shown (1) that some cases may run an afebrile course; (2) that in others the characteristic eosinophilia may be lacking, either throughout the whole course or for several

weeks after the onset of symptoms, and (3) that, rarely, the differentiation from typhoid fever may be rendered difficult by the presence of a strongly positive Widal reaction

Among other atypical clinical forms considered are (4) cases resembling

acute nephritis; (5) cases which simulate acute meningitis, (6) cases with conspicuous and alarming throat symptoms; (7) those simulating frontal sinusitis, and, finally (8) certain cases in which epigastric pain is the chief or only symptom

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# The Relation of Psychiatry to Medicine\*

By AUSTEN FOX RIGGS, M D , *Stockbridge, Mass*

THE relation of psychiatry to medicine has, until quite recent years, been very unimportant, extremely tenuous, and quite unsatisfactory. Psychiatry has been considered, and with considerable justification, a very poor relation of medicine. This conception of its status is, however, largely a thing of the past, and as psychiatry itself has advanced, so also has its relation to general medicine. As a matter of fact I am not sure that further improvements in this relationship, to be immediately expected, will not have to come from the other side of the fence, so to speak, that is, from general medicine itself.

Nevertheless psychiatry even now is too generally thought of by most medical men as a narrow specialty, concerning itself only with so-called mental disease. On the contrary it covers a much wider field. It deals not only with mental disease but with all disorders of thinking and feeling, whatever their cause, whether in diseased brains or healthy brains, with all degrees of amentia and dementia; and with maladaptations to life, whether due to inadequate mental equipment or to inadequate use of a normal equipment.

To be more definite and specific, psychiatry may be described as one aspect, or, if you prefer, a major expression of neurology, based in common with it upon the anatomy, physiology and pathology of the nervous system. Indeed these two, neurology and psychiatry, should always be hyphenated and thought of as one subject—neuro-psychiatry.

Far from being a narrow specialty, neuro-psychiatry is the broadest of all specialties, for just as the nervous system, which is its particular field, is the means by which all parts of the body are integrated and through which the body as a whole adapts itself to its environment, so neuro-psychiatry is the specialty which may often be used to integrate all other specialties.

The nervous system plays its important part in every disease, in every ill that flesh is heir to, and in the success or failure of every form of treatment. It seems obvious, therefore, that a specialty dealing with this great integrating system, with this all-important adaptor mechanism of the body, should enjoy the most intimate relation with general medicine. It has not in the dim past, but it surely will in the not too distant future, for medicine needs a full working partnership with neuro-psychiatry at least as badly as neuro-psychiatry needs such a relationship with medicine.

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There is no disease or disorder which does not in some degree affect the patient's emotional and mental life, nor is there any such condition which is not, in its turn, favorably or unfavorably affected by the patient's feelings and thoughts

Though the pathology of a given pneumonia may present a microscopically identical picture with many hundreds of others, the mental and emotional effect it is having upon a given patient is unique to him, and the effect of these personal reactions of his upon the course of his disease may be of the utmost importance. You might perhaps neglect the orthopedic or dermatological aspect of the case but not the psychiatric, which may make all the difference between success and failure in the treatment of the case

The patient with cancer of the breast may present the very same surgical problem as hundreds of thousands of others, but the significance to her of her disease, the significance to her of death, deformity, pain, and of every step of the proposed procedure will be in the aggregate unique, because it will be based upon her personality, her intelligence, her experience, her financial and social status, and the effect of her emotional reactions upon her physiological condition, upon her resistance to shock, indeed upon every item of the case up to and including its final outcome, may be profound. The gynecological aspects of the case may perhaps be safely neglected, there may be no reason for considering it from the aspect of any other specialty, save only psychiatry, but this side *cannot* be neglected with impunity

It may not be appropriate or even wise to call in a psychiatrist to aid in the treatment of some diseases, but the physician or surgeon should at least have the psychiatric attitude. In many cases neuro-psychiatry should not be considered so much a specialty as an aspect, and a very practical and important aspect, of medicine itself, for the psychiatric point of view whether in diagnosis or in treatment, considers the individual and not just the disease, values the aid to be enlisted from favorable emotional reactions, values the intelligent cooperation of the patient, and fears the untoward effects of adverse suggestion, adverse emotion, and ignorance, both on the pathological condition and on the efficacy of the treatment itself

As an example of the non-psychiatric attitude and of the great opportunities that may be lost by the consequent lack of intimate cooperation between medicine and psychiatry, I quote the following case

The Medical Staff of a great General Hospital combined to treat a supposed duodenal ulcer in a middle-aged woman. She was suffering from an involutional depression with fixation of symptoms on her vegetative activities, as is often the case. The ulcer was never quite satisfactorily proved, but it was most sedulously and skilfully treated and cured. The opinion of her medical advisers was that the depression was due to the supposed ulcer and when that was cured the depression it had caused would disappear. They were surprised and genuinely chagrined that in spite of the good effects locally of the treatment, the patient took no interest in either

procedure or result Discharged cured, she went home and died of her psychiatric disease—by taking poison The necessity of the psychiatric point of view in this case needs no further comment

Today the director of this great hospital has a psychiatrist on his staff, not as a consultant but as a regular attending physician who makes rounds with him, a cooperative arrangement which marks progress, of benefit not only to the internist and the psychiatrist but to every patient whom they serve

As an example of how well such an arrangement works out in practice, the following case from another metropolitan hospital will serve Here for the past two years a psychiatrist has been a member of the attending staff

A young man was operated on for gastric ulcer A gastro-enterostomy was done The surgical recovery was excellent but the patient continued his post-operative vomiting There was no apparent cause for this phenomenon Every sort of medical treatment was tried without success No sooner had the patient swallowed a few spoonfuls of his carefully prescribed diet than up they would come again Toward the end of the week following the operation, the psychiatrist was asked to take a hand and see if he could do anything before an exploratory operation was resorted to He found that the young man was highly neurotic, very suggestible and had somehow gathered the distinct belief that the purpose of the operation was to close the exit of the stomach and that therefore the only way left for

food to get out of it was to come up. A simple explanation of the operative and anatomical facts, and of the effect this erroneous belief had had in continuing the vomiting was all that was required to ensure the patient's smooth and uneventful recovery

Let these two cases suffice to illustrate not only the great advantage of a close relationship between psychiatry and medicine but that it may often become a factor of the utmost importance to the very life of the patient

There is an enormously large class of cases in which neuro-psychiatry is not only important but necessary to medicine I refer to the so-called functional disorders It has been conservatively estimated that these constitute a very substantial majority of all cases seen in the medical out-patient departments of hospitals, as well as in the private consulting rooms of general practitioners These disorders are of psychogenic origin with very few exceptions They not only call for psychiatric understanding but are the very meeting ground of psychiatry and medicine

An over-active colon may be due to a primary disturbance of its flora, but thousands of cases of so-called colitis are simply physiological expressions of an emotional state In short, the "colitis" very often is merely an active, though sometimes obstructive, symptom of a far-reaching emotional disorder.

Likewise, the cause of some cases of hyper-thyroidism may be found in the patient's emotional life, rather than in a primary disturbance of one or more of his endocrine glands

Many functional cardiac disturbances are notoriously typical neuroses

In all of these cases the relation of psychiatry to medicine is of utmost importance, especially to the patient. Too often even in these modern days, the patient suffering from a neurosis goes from specialist to specialist with but temporary relief, only to fall finally into the more astute and less scrupulous hands of the charlatan because he, even though unscientifically and "as through a glass darkly," sees the psychiatric problem involved. When he too through greed and ignorance perhaps may lose his hold, and the neuro-psychiatrist finally gets his chance, the case by that time has reached a most unfavorable stage, for the patient has often lost faith in all doctors, in all science, and is mighty apt to take to pseudo-science, pseudo-religion or again to the best advertised charlatan.

The treatment of all neuroses and more obviously of all psycho-neuroses is of course primarily a psychiatric job, but the internist should at least be able to make a tentative diagnosis and help the patient to obtain suitable treatment promptly. Too often is this diagnosis made only after exhausting all and sundry possible medical and even surgical methods, and even then it is only reluctantly accepted and often with considerable undeserved contempt for the patient. Such a negative diagnosis, it might be noted in passing, is really no diagnosis at all. To say that a patient, because no other disease can be pinned on him, must therefore have a neurosis is not even logical. A neurosis is a real and recognizable disorder. It always has a

cause, always functions in a more or less typical way, and an absolutely positive diagnosis should always be made. It cannot however be made without due consideration of these factors nor without adequate study of the patient's personality. Furthermore, medical treatment of a neurosis on a merely symptomatic basis does the patient absolute harm, for it places all the emphasis on the symptoms and tends to fix the neurosis and further entrench it against therapeutic attack. Obviously these cases should not be tinkered with by the internist even though he may have made a diagnosis, for they require all that the most skilful psychiatrist can give them. Here is where psychiatry can help medicine by assuming the major diagnostic and therapeutic burden, and here too is where medicine can co-operate most fully with psychiatry in evaluating the concomitant physical disorders and finding their treatment.

There is another function in relation to general medicine which neuro-psychiatry seems to be in a fair way of having to assume. I refer to the function of family adviser, which office used to be so well filled by the old-fashioned family physician and which now, by his lamented disappearance, is left practically vacant. The need is still there, indeed it is greater than ever in this day of extreme specialization. It is not satisfied by the most scientific and complete modern diagnostic survey by a group of specialists. Usually there is no one in the group or out of it who is sufficiently familiar with the patient's personal and family condition and problems to head the whole affair and steer the patient ac-

cording to his particular personal needs. By the very nature of his field the neuro-psychiatrist must know all that can be gleaned of the patient's family history, direct and collateral, he must have all the available facts of the patient's familial, social and financial conditions, as well as a full medical history. He is thus usually supplied with the necessary data. Unless some other more able and better fitted candidate for the position of family adviser appears, I think it most likely that the job will fall to the neuro-psychiatrist. Indeed I could quote numerous incidents from my own experience where this has already happened. In some cases the neuro-psychiatrist becomes the family physician because he has had to assume control in order to guide the patient, or the whole family, out of the labyrinth of unrelated and uncoordinated specialties. Sometimes he has been requested to assume the rôle, sometimes he has no doubt been accepted only "*au faute de mieux*." However that may be, the gap that the disappearance of the old time family doctor has left presents a problem which a closer relation between all specialties and particularly between psychiatry and medicine should go far toward solving.

But after all, that a closer relationship between psychiatrist and internist, between neuro-psychiatry and general medicine is greatly to be desired can hardly be doubted. It is so nearly self-evident that it needs little argument. But how can this be accomplished? How can the progress, already begun, toward a better relationship be accelerated?

The following possibilities of improvement suggest themselves.

First —Let us begin at the beginning. Let us teach more neurology and psychiatry in the medical schools. Already in one of our leading schools these subjects are allotted slightly greater time in the curriculum than surgery. This is progress worth noting and an example worthy of emulation.

Second —I would suggest following the good examples already set, by appointing neuro-psychiatrists on the attending staffs of hospitals wherever possible,—and using them. This advance would naturally be initiated by the internists in charge.

And Lastly —I suggest that slow but sure method,—the education of the profession at large.

This may be done,—

First —By including papers on neurology and psychiatry especially in relation to general medicine, at meetings such as this.

Second —By including papers on general medical subjects, with especial reference to their relation to neuro-psychiatry, at meetings of neurologists and psychiatrists. The initiative should of course come from the latter.

Third —By urging the members of the medical profession throughout the country to read the reports and journals of the mental hygiene organizations, so that they may familiarize themselves with at least the statistical facts in regard to the prevalence and increase of neuroses and mental diseases and disorders in this country at the present time. Few general medical men are aware of these facts. For



instance, how many know that more hospital beds are occupied today by those suffering from mental and nervous diseases than from all other diseases combined or that the number of unhospitalized psycho-neuroses is probably by far the greatest of all? A few such facts would make it quite clear to everyone that at least more

than half of the enormous problem which modern life presents to medicine falls into the field of neuro-psychiatry, and that, furthermore, both neuro-psychiatry and medicine need all the help that either can get from the other to make headway against this problem, which neither can solve alone

# Psychiatry's Part in Preventive Medicine\*

By ARTHUR H. RUGGLES, *Providence, Rhode Island*

UP TO about fifteen years ago, psychiatry did very little that was actively preventive, its concern was largely with classification, the improvement in methods of treatment and the discussion of heredity vs environment. With the advent of the Wasserman and the treatment of General Paresis with the arsenicals, and with the more general employment of lumbar puncture, Psychiatry learned that no case of syphilis could be considered permanently immune from neuro-syphilis unless repeated negative blood Wassermans were obtained following intensive intravenous therapy, and more especially unless it was determined over a period of at least two years following infection that the cerebrospinal fluid was not invaded. This was the beginning of a preventive effort regarding General Paresis and, while sufficient statistical study has not yet been completed, there seems to be evidence to show that in some mental hospitals the cases of General Paresis have in ten years been reduced from 10 to 12 per cent of all admissions to 8 to 10 per cent. I will not attempt to analyze this decreased percentage of G. P.'s, but believe it is in part due to the employment of preventive steps insisted upon by the syphilologist and psychiatrist.

At the time of the Great War the country was aroused from its self-complacent attitude by finding many thousands of our youth unfit for military duty by reason of mental defect, or of nervous or mental disease. In the years since the war we have seen nearly every state improve their facilities for the segregation of some of the feeble minded and for the community treatment of others. This is a step that in another generation should lessen the propagation of the mental defective, but in this particular direction we still have a long way to go and much to learn regarding prevention. The misnomer "Shell Shock" brought to the attention of layman and physician alike many cases of psychoneuroses that would otherwise have gone without understanding or treatment, and so we have recognized and cured many minor psychoses, as they have been called by some writers, and thus tended to reduce the number of nervous invalids in the community.

In the study of personality types we have come to recognize the schizoid and the syntonik, and thus we are better enabled in some cases to avoid the particular situations in life that would tend to push these individuals on into frank psychoses.

Yet you may say, "What evidence is there that psychiatry has done anything in preventive medicine when the total numbers admitted to mental hos-

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pitals are yearly increasing?" but so are the stress and strain of modern life, and so are the number of mentally sick persons admitted to hospitals who formerly roamed the streets or were secluded by the families at home. There are more general hospital beds filled with patients than there were ten years ago, but that does not mean that more people are annually sick, for we know typhoid fever, tuberculosis, diphtheria and many other diseases are much decreased today. It may take another quarter of a century before we can definitely demonstrate results in the prevention of mental disease, but that psychiatry is even today beginning to play an active part in preventive medicine I believe few can deny.

One of the preventive forces borrowed by the psychiatrists from the medical clinic, and developed to a very high degree, is the psychiatric social worker who investigates the social environment of our cases, who helps in the adjustment of the environmental situation when it is indicated as a measure of treatment, and who especially follows up cases leaving a mental hospital for a very long period of time. The assistance of the psychiatric social worker has been very great and serves as an indispensable part of the psychiatrist's armamentarium in his preventive measures. The psychiatric social worker has a recognized place in every well organized mental hospital, out-patient department and child guidance clinic.

Today every psychopathic hospital, and many of our state and private mental hospitals, have out-patient departments where large numbers of the

psychoneuroses and psychoses are treated. Here the psychiatrist, the psychologist and the psychiatric social worker examine, investigate and carry on the treatment of psychoneurotics and of incipient psychoses, such as mild depressions, hypo-manic states, early schizophrenia, general paresis and other types of cases in which institutional treatment is not indicated, and thus many psychotic cases are readjusted or stabilized sufficiently so that they never need to go into a mental hospital. More and more the work of the mental hospital lies in the field of prevention and undoubtedly can best be met by the development of out-patient facilities. And in the mental hygiene movement as a whole, and perhaps more especially in the mental health program of individual states, no better policy could be established than that of for each dollar spent for building an equal amount be devoted to prevention.

Perhaps the best organized evidence of the attack on nervous and mental disease is in the schools of our country, and especially in the Child Guidance Clinics. At least fifteen large cities of this country have well organized Child Guidance Clinics where the pre-school and school child are thoroughly examined and treated by the psychiatrist, the psychologist and the psychiatric social worker. Most of the school systems of our cities, and many towns, have made provision for psychiatric examination of problem children. Here in Massachusetts there is a state law that requires the examination of all school children three years or more retarded; this is carried out by the staff physicians of the State

Hospitals. We know that 75,000 new cases are being admitted to mental hospitals each year, at the present admission rate that means 750,000 in the next ten years. From our knowledge of the average age of these patients on admission, we know that the majority of these prospective mentally sick are in our Grammar Schools and High Schools. The school psychiatrist is certainly in a strategic position to do preventive work, for we know definitely that certain mal-adjustments of personality not recognized or wrongly treated mean a larger psychosis, and that these cases can in many instances be so directed that nervous invalidism or the frank psychosis is avoided.

Perhaps one of the greatest contributions made by Psychiatry to Preventive Medicine is the insistence upon the understanding of the patient as a total human being with emotions as well as tonsils, with conflicts as well as a heart, and with thwarted purposes as well as a gastro-intestinal tract, so that we do not diagnose heart disease without understanding the total personality of the patient whose heart interests us, or do not take out the patient's tonsils to cure a psychic conflict. An illustrative case may make clear the point I wish to emphasize: a man of 32 came under my care because he had become afraid to leave his house unaccompanied or to be left alone in his home. For two years he had made his rounds of medical men with the result that the following diagnoses had been attached to him: Deviated nasal septum, eye-strain, gastroptosis, mucous colitis, varicocele and floating kidney. Is it any wonder

he was afraid to be left alone? All of these conditions may have presented themselves to the examiners at various times, but a series of diets, belts, irrigations and operations could only have exaggerated his condition until the primary difficulty, which was a definite mental conflict, was understood and removed by treatment. I may have used an extreme case for illustration, but there are far too many nervous invalids being created today because the medical man fails to investigate mind as well as body, and then to evaluate the disorders that may be present in both fields. You may say, "But the psychiatrist thinks all disease is located in the mind", not at all, the well staffed psychiatric clinic finds that a large percentage of mental defect has its basis in birth injuries, deafness, visual disorders and endocrine dysfunction. The psychiatrist knows that certain neurasthenic and hysterical symptoms may be the earliest manifestations of a brain tumor. Focal infections are not neglected, in fact, perhaps some of us have over-emphasized their importance. In a high percentage of all our cases we find causative factors in the blood picture, in the gastro-intestinal tract, in the gall bladder and in impaired kidney function. I shall never forget a delirious patient sent from the medical wards of a general hospital to a psychiatric hospital for care. A few days later the mental hospital made a diagnosis of central pneumonia, whereupon the referring physician at once said, "Of course, you will send the patient back to us for treatment of his pneumonia!" When it was explained that the physi-

cal disease would receive adequate treatment, and the mental symptoms better treatment than the general hospital could provide, the medical man expressed surprise, but the patient soon recovered in our mental hospital, and I honestly believe that many delirious patients die in the general hospital who would recover in the mental hospital, because of better understanding of the treatment of delirious states on the part of psychiatric nurse and doctor. Recently, in one of our New England mental hospitals, a case of undulant fever was diagnosed by a staff physician, this being the first case recognized in the whole state, so that the mental hospital cannot be accused of being medically unobservant or unprepared

The psychiatrist today has a recognized place in the medical departments of schools, colleges and industry, in which fields the work is largely preventive

It seems to me that psychiatry still has a very great contribution to make to preventive medicine in the field of a better understanding of the causation of some of the recognized mental diseases which, at the present time, fill a large proportion of our mental hospital beds. Since the days of Kraepelin's classification, which began more than a quarter of a century ago and which has been modified and improved, but not essentially changed, there have been, with the exception of the treatment of general paresis, the more careful correlation between physical and mental findings and the analytical approach to some of our cases, almost no real contributions to the understanding of the etiology of

the psychoses, and it is high time that every psychiatric hospital with its wealth of controlled material should establish laboratories for an intensive attack on such important mental diseases as schizophrenia and the manic-depressive psychoses. Until this is done we will, I am afraid, have to concentrate our attack on mental diseases largely upon our attempts to adjust personality at earlier age levels, and to individualize and intensify our treatment of cases. A great number of research workers concentrating with all modern methods upon the study of a large group of psychoses whose etiology is at the present time unknown may, in the next quarter of a century, bring to medicine a better understanding of the essential factors underlying thousands of mental diseases, which would enable medicine to intelligently reach a large percentage of cases today occupying hospital beds

Let me close with an illustrative case from my college mental hygiene experience. A freshman in college became depressed, unable to sleep and unable to study. He was sent to the Medical Hospital Department where it was found that he had no physical disease. His father had for years suffered from a manic-depressive psychosis, and the boy had always feared he might become a victim of the same disorder, so quite naturally when he became fatigued with hard study and working additional hours to earn money, he could not concentrate, his grades fell and he became depressed. When he saw the psychiatrist he was convinced that his father's future was before him. A readjustment of his working hours, better diet and general

physical hygiene, together with explanation and encouragement soon dispelled the depression, the boy got well and finished his year with high marks. In his second year emotional over stimulation of fraternity activity and competition for a position on a college publication brought on an attack of acute excitement that was recognized as a manic attack. Immediate rest in bed with mild sedatives promptly cleared this up, but it was felt that two mental upsets in two years made the situation serious. He was advised to go into the country for six months, which he did, and then advised to transfer from a large city college to a small college in a country town, here, competition of all sorts was less, reducing mental stress and strain, and he was graduated two years

ago. He is now holding a good position (again without too much stress and strain), has had no recurrence of his trouble, and I will venture to predict will not, if he obeys the rules of mental health that apply to his make-up.

Without mental hygiene I am sure our mental hospitals would have added another to their list of cases, and, so, I believe that psychiatry is already contributing something to preventive medicine, and will have much more to contribute, if medical education trains all physicians to understand and treat the whole human being and not simply a diseased section of a case, and if psychiatry itself develops a group of physicians intensively laboring to better understand the causes of the mind diseased.

## Relation of Streptococci to Influenza\*

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MUCH difference of opinion exists as to the causative organism or organisms of epidemic influenza. The general belief is that it is caused by the influenza bacillus, although many authorities are of the opinion that while this organism may be related to the infection, it is not the primary cause. With the development of our knowledge of the wide variety of clinical entities produced by the streptococci, different authorities have recently suggested that these organisms may be responsible for this disease. An opportunity was offered us during the recent influenza epidemic at Ann Arbor (Nov 1928 to Feb 1929), to carry out a bacteriological investigation of a group of influenza cases. The results of this investigation as well as more recent views of the causative nature of influenza will be discussed in this article.

If we look back to the influenza pandemic of 1890-1891, we find the description of the disease prevailing at that time described by Lichtenstern<sup>1</sup> as follows: "The typical influenza consists in a sudden fever, which is initiated by a chill or chilly sensation—lasting from one to several days, is

associated with severe headaches (especially in the frontal region), vertigo, pain in the back and legs, disproportionately severe prostration and loss of appetite. After 10-12 hours, perspiration ensues and in 24-48 hours, the fever has usually subsided in many of the patients, leaving them with great weakness and with pains in muscles and joints which disappear in a few days. Symptoms of catarrhal inflammation of the respiratory tract often supervene upon the above manifestations."

Again, Zinsser<sup>2</sup> describes the cases of the 1918 pandemic in the following manner: "The early cases were clinically so uniform that a diagnosis could be made from the history alone. The onset was almost uniformly abrupt. Typical cases would become ill suddenly during the night or at a given hour in the day. A patient who had been perfectly well on going to bed, would suddenly awake with a severe headache, chilliness, malaise and fever. Others would arise feeling perfectly well in the morning and at some time during the day would become aware of headache and pains in the somatic muscles. Occasionally there was nausea. A few of the patients could state the exact hour at which they were taken ill. There were, of

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course, some cases in which the onset was more gradual "

Those who had occasion to see the influenza cases at the University Hospital will immediately recognize the above description as fitting these patients. The cases were invariably characterized by a sudden onset, fever, headaches, generalized aching and marked prostration, occasionally also nausea and anorexia. The course in the uncomplicated cases was usually a short one, the patients having a high temperature,  $101^{\circ}$  to  $104^{\circ}$  at the onset, which rapidly came down to normal within one to three days. The patients felt much improved on the third or fourth day and were anxious to return to work, although the majority of them experienced definite fatigability upon exertion, for a considerable period of time.

The physical examination of a typical case presented striking and characteristic features. The patient appeared prostrated. The face was usually suffused and the eyes were watery, glistening and occasionally reddened due to the injection and inflammation of the conjunctivae. The throat examination revealed the fauces to be markedly reddened, glistening and usually dry. There was a sharp line of demarcation of the redness at the junction of the soft and hard palate around to the base of the anterior pillars. The tongue was characteristic in a great majority of cases—being usually furred, with the edges and tip clean, reddened and showing red swollen papillae.

In several cases, there was an erythematous rash of an intense hyperemic character on the chest and neck

suggesting very strongly a scarlatini-form eruption. This rash was so characteristic in about six or eight cases that they were sent to the contagious hospital with the provisional diagnosis of scarlet fever. At least two patients who had very severe infections, with a pneumonia complication in one and an acute pansinusitis in the other, showed desquamation of the hands and feet during convalescence. Indeed it was this clinical picture which suggested a bacteriological study of these cases. It was believed that the *Streptococci scarlatinae* or closely related streptococci were possibly playing an important etiologic rôle in these so-called influenza cases.

#### BACTERIOLOGICAL STUDY

The general plan of this study was to determine the predominant type or types of organisms found in the throats of influenza patients as compared with those found in non-influenza patients and in healthy individuals. When the colonies of any given organisms grown on blood agar plates were found to the extent of 50 per cent or more of the total growth, the organism was considered as predominant. It was believed that the presence of isolated colonies here and there of any given organism could not be interpreted as being of special significance since cultures of so-called normal throats frequently show such isolated colonies. Blood cultures were made on all influenza cases. Of these, only one showed positive findings, in the nature of *streptococcus hemolyticus* \*. In a few of the influenza

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\*This was a post operative case which developed influenza complicated by bronchopneumonia and later septicemia.



cases showing complications, cultures were also obtained from the infected foci. A total of 142 cases was studied. These included 43 influenza patients, 11 influenza post-mortem examinations, 63 non-influenza patients and 25 student nurses who gave the

history of not having had any respiratory infection or other illness during the past year

The bacteriological findings are illustrated in Table 1. Of the 54 influenza cases, 44 showed a predominance of hemolytic streptococci and 7 of strep-

TABLE I  
INCIDENCE OF THE PREDOMINATING ORGANISMS IN INFLUENZA CASES AND CONTROLS

No. of cases	Types of Cases	Hemol Strep	Strep Viridans	Pneumo cocci	Micro Catarr	Variety of Organisms
43	Influenza patients	33	7	1	2	0
11	Influenza post-mortem exam	11 (100%)	0	0	0	0
63	Non-influenza patients	6	12	0	3	42
25	Healthy individuals	0	0	0	0	25
		% Streptococcus				
		{ influenza cases				94%
		{ control cases				20%

tococcus viridans. A total of 51 cases or 94% thus showed predominance of streptococci. The remaining showed a predominance of pneumococcus in one and Micrococcus catarrhalis in two. It is interesting to note that one case showed a pure culture of hemolytic streptococcus one day, in a second culture streptococcus viridans predominated, and a third culture again showed pure culture of hemolytic streptococcus.

Of the 88 control cases, 6 showed predominating hemolytic streptococcus and 12 showed a predominance of Streptococcus viridans. Considering the streptococci as a whole, the total incidence in these cases was 20 per cent. These control cases included 63 non-influenza patients suffering from a variety of diseases in the medical and surgical wards of the University Hospital, and 25 healthy individuals. All of the latter gave a negative history for previous influenza infection, and no upper respiratory infection

within the last year. None of the throat cultures in these cases showed streptococci in predominance but showed a variety of organisms typical of normal throats.

It may be of interest to mention case P. A. He was a cardiac patient on the medical ward who had entered the hospital about two weeks previous to the day when control cultures of the non-influenza cases were taken. The throat culture showed 100% hemolytic streptococcus. Twenty-four hours after the cultures were taken, the patient showed typical symptoms and signs of influenza. Two days later he showed signs of bronchopneumonia and on the fifth day after the onset of the influenza symptoms, the patient died. No post-mortem examination was made.

Although the total number of influenza cases studied was relatively small, the high incidence of the streptococcus isolated would suggest that these organisms are etiologically related to this

infection Whether they are the primary or the secondary agents, it is not possible to say. It is of interest in this connection to recall that Donaldson,<sup>3</sup> who has made an extensive bacteriological study of the influenza pandemic of 1889 to 1892, concludes

- "1 That no type of organism was found common to all influenza cases
- 2 Not only did one or the other of the organisms predominate in certain localities, but they were often found in pure cultures, causing the observers to hail it as 'the' cause of influenza
- 3 Moreover, the bacterial balance in one locality was not always the same—at one period of the pandemic, the prevailing organism might be a streptococcus, at another, the pneumococcus
- 4 Many of the organisms possessed pleomorphic characters "

With the announcement by Pfeiffer of his discovery of the influenza bacillus in 1892, bacteriologists throughout the world directed their attention to the study of this organism in connection with influenza. The result was that during the influenza epidemic of 1918, practically all effort was con-

centrated on the Pfeiffer organisms. In spite of this effort, the percentage of influenza cases showing Pfeiffer bacilli was relatively small. Donaldson<sup>3</sup> made a study of the bacteriological reports published in England, Germany, France, America and other countries of the 1918 influenza pandemic. According to this investigation, of 19,145 examinations made on influenza patients, only 34.4% showed the Pfeiffer bacillus. Of 3,056 post-mortem examinations, about 40% showed this organism. A summary of Donaldson's figures relating to this pandemic is presented in Table 2.

It is seen from this table that the Pfeiffer bacillus was found in 30.3% of the healthy individuals and that the percentage of positive findings during the epidemic was higher in those suffering from non-influenza disease than those suffering from influenza. Based on these figures, Donaldson concludes "Whatever was the cause of influenza, it was certainly not Pfeiffer's bacillus. If the infection was due to a common virus, the Pfeiffer bacillus was not even the most important secondary invader."

It was unfortunate that the pneumococcus and streptococcus groups were not studied with the same thoroughness in the 1918 pandemic, as was the Pfeiffer bacillus. This was due to the erroneous view that the latter was the

TABLE 2  
INCIDENCE OF PFEIFFER'S BACILLUS IN INFLUENZA AND CONTROL CASES DURING PANDEMIC, 1918-1919, AND INTER PANDEMIC PERIOD

	Interpandemic Period	Pandemic Period
Influenza	29.2%	35%
Non-influenza diseases	40%	49%
Healthy individuals	18.6%	30.3%

primary cause and that all other bacteria were secondary invaders. Accurate figures were therefore not available, since many observers had either ignored the other organisms or had casually stated that they had not been noted. In Donaldson's<sup>3</sup> opinion, "the pleomorphic streptococci strains were more important pathological agents, as proven by serological tests. Many were highly pathogenic for animals, were more consistently virulent and resulted in illness more like influenza than that caused by Pfeiffer's bacillus. Hence, the pleomorphic streptococci behaved in a more virulent way and were found in a greater percentage of the influenza cases and should therefore rank more importantly even as secondary invaders, than Pfeiffer's bacillus. Insofar as the pleomorphic streptococcus was present in a far higher percentage of cases than Pfeiffer's bacillus, it has an even better claim at being *the* cause of influenza. Of course, in absence of sufficient data to prove Koch's first postulate that it must be found in all cases, this claim cannot be maintained." It is of interest to note that Pfeiffer's original studies were based on a total of only 31 cases.

Zinsser,<sup>2</sup> in a review of the Etiology of Influenza, states that the pneumococci and streptococci are probably not etiologically related to influenza. His reason is that since these organisms habitually inhabit the upper respiratory tract, they would be frequently isolated from influenza patients. He also concludes against the Pfeiffer bacillus theory, his evidence being

- 1 Frequent failure of competent bacteriologists to find it

- 2 The presence of the bacilli in the throats of normal individuals
- 3 Their presence in pathological conditions not influenzal
- 4 Frequent presence as complicating invaders as in Whooping Cough, Measles, etc
- 5 The multiplicity of strains
- 6 The infrequency of blood culture findings
- 7 The unsuccessful attempts to produce the disease in human beings with pure cultures

Modern bacteriology gives us a possible clue as to the relation of the streptococci to influenza. It has become recognized in recent years that bacteria are capable of passing through a life cycle and that at certain stages in this cycle, not only their morphology, but their physiological, cultural, serological and antigenic characters may undergo change. May it not be possible that the streptococci when in a special cyclogenic stage are capable of producing the syndrome of influenza?

Microbic dissociation has recently been summarized comprehensively by Hadley<sup>4, 5</sup>. Dissociation of bacteria most frequently occurs as a result of changes in their environment. Several cyclogenic forms have been isolated from single strains of organisms including the "R" or non-virulent form, the "S" or virulent form and, as is being attempted now, the "G" or filtrable form. In former days, pleomorphism meant to the orthodox bacteriologist that he was dealing not with one organism but with a mixture of organisms—possibly due to faulty technique. The modern bacteriologist, however, looks upon pleomorphism as

natural variations in the life cycle of the organism

This conception of cyclogenic variation in organisms according to Hadley is destined to change our point of view of the etiology and epidemiology of infectious diseases. Etiologically, the virulence of a given strain of organisms depends on the predominance of the "S" or "R" forms. The same is true when considering the agglutinating properties of an organism. If, as occasionally occurs, a given typhoid strain is not agglutinated by anti-typhoid serum, it is no longer interpreted as an anomalous reaction but as a reaction with a cyclogenic form of the typhoid organism having different antigenic properties.

It is possible that the onset of an epidemic is caused by a change in an organism or in organisms from their non-virulent or inactive form to a virulent virostage, and that the remission of an epidemic is the passing into a non-virulent form. In the treatment of disease, future efforts will probably be directed toward the control of the cyclostage by studying how, in what sequence, and under what conditions of environment, cyclogenic variations have been and can be produced.

Applying the above bacteriological conception to influenza, the fact that 94% of the cases showed predominating streptococci would suggest the possibility that some dissociated form of these organisms—conceivably, a filtrable virus form—is the disease producing agent. Conditions of which we are as yet ignorant may be responsible for producing this dissociated form which initiates this disease. The

only observations deserving serious consideration that influenza is caused by a filtrable virus are those of Olitsky and Gates<sup>6, 7, 8, 9</sup>. They have isolated from the nasopharyngeal secretions a minute filtrable bacillary organism which they call "Bacterium pneumosintes". Their data warrants further investigations of this organism.

In view of the clinical similarity of this disease to other entities caused by the streptococcus and because of the high incidence of the streptococcus in the cases examined by us, we feel that further study of the organism, perhaps from the point of view suggested by Hadley, is indicated.

#### SUMMARY

A bacteriological study was made of 142 individuals during the recent influenza epidemic at Ann Arbor (Nov 1928 to Feb 1929). Of 54 influenza cases, 94% showed a predominance of streptococci, these consisting largely of the hemolytic form. Of the 88 control patients, 20% showed a predominance of streptococci. Studies on influenza have been heretofore directed largely to the Pfeiffer bacillus; paying comparatively little attention to the streptococcus group. The clinical picture of influenza and the high incidence of streptococci found in this study warrant further investigation of this organism in relation to this disease. When considering the dissociation which organisms undergo under different conditions, it is conceivable that the causative organism of influenza might be the streptococcus in some dissociated state, possibly a filtrable state.

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# Lead Poisoning From Snuff\*†

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**N**OTWITHSTANDING education, publicity, and restrictive measures lead poisoning has become the chief industrial hazard. Since compounds of lead frequently contaminate drinking water, beverages, cosmetics and a variety of other substances used by mankind, it has become equally as important a factor in causing distress and sickness among the non-industrial population. New sources of lead poisoning are constantly being uncovered so that it behooves the Medical Profession to be forever on the watch for this important disease and its manifestations. Within the past year another source of lead poisoning, while by no means new, should be newly emphasized in this country.

Model<sup>1</sup> in 1784 first drew attention to the possibility of lead poisoning from snuff-tobacco. In 1843 Otto<sup>2</sup> of Copenhagen reported two cases, one of which was fatal. The victim was a botanist and scholar, who suffered from obstinate constipation, abdominal cramps, headaches and who finally became comatose and died. Not until after his death was lead poisoning suspected and then an analysis of the

brand of snuff he was in the habit of using, showed considerable lead. For some years following this a number of articles appeared in the foreign literature dealing with this source of lead poisoning, for in 1886 Billings<sup>3</sup> collected a total of 23 references, including 5 cases reported by Mayer<sup>4</sup> and 19 cases by Sonnenkalb<sup>5</sup>. About this time Garrod<sup>6</sup> in a clinical lecture on "Lead Poisoning" emphasized the possibility of lead poisoning occurring in warm climates when moist snuff is packed in lead covered boxes. He reported a case of an Englishman who had just returned to London from India on account of an illness, the cause of which was traced to lead found in snuff. In 1904 McCaw<sup>7</sup> added six more references, which included an interesting case of aphonia caused by lead poisoning from snuff reported by Ormsby<sup>8</sup> of New York. In 1912 Stadler<sup>9</sup> of Switzerland reported that a certain metal-foil wrapper contained 89.0% of lead and the moist snuff contained 175-190% of lead. Habitual use of this brand of snuff by a woman caused fatal intoxication. In 1918 four cases were reported in America, three cases by Uttal<sup>10</sup> of New York City and one case by Bauer and Ropes<sup>11</sup> of Boston. All in all about forty cases have been reported.

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\*Read at the Boston meeting of the American College of Physicians, April 11, 1929.

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There are three possible causes for lead in snuff tobacco: (1) adulteration of manufacture, (2) lead wrappers, and (3) lead compounds used in manufacture.

The manufacture of snuff consists in cutting tobacco leaves and filling with salt water, and leaving them to ferment in a special chamber for some months. Then the tobacco is ground to a powder, mixed with gum and put into a closed wooden chamber to undergo a second fermentation process. The tobacco, about two-thirds of the weight, and the mastic and citric acids in the tobacco, while the acid and bases excised leaves are abundant in the snuff. Various flavors are added to give scent. Quinine is often used to give a biting, desiccating effect. Formerly, lead oxide and chromate were added to give a lighter color and greater bulk, and thereby increase the sale value. Snuff is packed and marketed either in a dry or moist state, depending upon the amount of moisture added during the fermentation. In 1849 Hassel<sup>1</sup> examined 13 kinds of snuff, nine brands contained lead chromate in amounts varying from 1-1.5%; three specimens contained lead oxide. Since tobacco products do not come within the Federal Food and Drug Acts there is no adequate legislation to prevent adulteration at the present time.

Another source of lead in snuff and the one most referred to in the literature is due to the usage of lead-foil for wrapping and lead-tin boxes for packing. Stadler<sup>2</sup> (already referred to) reported 89% of lead in a metal-foil wrapper used for snuff even though the Swiss law prohibits a con-

tent greater than 1%. Wicke<sup>3</sup> found that the outer crust of snuff packed in lead-foil contained up to 27% lead even if the foil was lined with tin on the side. When the snuff is damp or contains acetic acid, absorption of the lead from the wrapper is apparently increased.

The third possible source of lead in snuff is due to the fact that lead-arsenate is used rather extensively as an insecticide in the growing of the chief types of tobacco used in the manufacture of snuff.<sup>4</sup> 1927 Remington<sup>5</sup> examined a large number of brands of American smoking and chewing tobacco and found arsenic to be invariably present in quantities many times greater than the amounts cited as being permitted in foods. It is possible that the source of the arsenic was due to the arsenate used in the plant spray and that lead may also find its way into tobacco for the same reason.

During the past year and a half I have seen four cases of lead poisoning from snuff. All were middle aged white women admitted to the charity ward of John Sealy Hospital. Analyses of the snuff, feces and urine of these patients showed lead. All chemical analyses were made by Professor B. M. Hendrix of the Department of Biological Chemistry. The patients all used the same brand of snuff which we believe was adulterated with lead chromate. The samples examined were marketed in glass jars.

The first case will be considered last. Case No. 2 has been free from symptoms now for about a year since she stopped taking snuff. Case No. 3, shortly after entering the

hospital died from an inoperable carcinoma of the cervix, hydronephrosis and uremia. She gave a history of taking snuff for 20 years. Twelve years previous to entering the hospital she had been advised to take radium treatment for her pelvic condition. What the diagnosis was at that time could not be determined. Post mortem examination confirmed the clinical diagnosis and a short while after the organs had been preserved in formalin it occurred to us to test certain of the soft tissues for comparative lead content. Analysis of the liver tissue showed 3.31 mgs of lead per 100 gms of tissue, heart muscle showed 4.42 mgs of lead per 100 gms of tissue, the carcinoma contained 7.34 mgs of lead per 100 gms of tissue. Not enough of the cancer was available for a duplicate determination, but we feel that the proportion of lead found in these tissues is reasonably correct. This suggests a greater affinity for lead on the part of carcinomatous tissue as compared to other soft tissues, but requires further investigation. Case No. 4 is in the hospital at present. She came in complaining of weakness, abdominal cramps and pains in her limbs. The snuff this patient was taking showed on repeated analysis 0.35% of lead chromate, or 0.224% lead.

#### REPORT OF CASE No. 1

November 4, 1927, Mrs. L. K., an Irish-American housewife, aged 44, came to the John Sealy Hospital complaining of weakness and vomiting.

Following an attack of "influenza" six months previous there had been increasing soreness and progressive weakness in her lower limbs. For two months there had been attacks of severe epigastric pains which

were referred to the back. With the pain was nausea and vomiting irrespective of meals, until finally she was unable to keep anything on her stomach. Besides this there had been dizziness, increased thirst, constipation, oliguria, and edema of the feet. For some time her sense of taste had been impaired. At the beginning of her illness her weight was 250 pounds, at time of admission it was 180 pounds.

She had measles, mumps and typhoid fever when a child and at one time she swallowed lye, which resulted in an esophageal stricture, for which numerous dilatations were performed. At the age of 18 an "abscessed ovary" was removed. All her life she had drunk a fair amount of beer and for the past 2 years considerable whiskey. She had never been pregnant.

Physical examination showed a middle-aged white woman, apprehensive with a pained expression and pasty appearance. Teeth were dirty and the gums showed advanced pyorrhea. Tongue was coated, and the sense of taste for sweet and sour was impaired over the anterior two-thirds.

Cardio-respiratory system was normal except for hardening of the arteries and a soft blowing systolic murmur localized at mitral area. Systolic blood pressure was 120, diastolic 86. There was generalized muscular weakness. The lower limbs were flabby and extremely tender to touch over calves and thighs. Knee jerks absent. All the other reflexes were normal. Pelvic examination showed atrophy of vagina and uterus.

The urine was acid and showed a low specific gravity and an occasional hyaline cast. No albumin or sugar present. A satisfactory gastric specimen could not be secured. The vomitus showed bile stained mucous and little else. Red cell count was 4,350,000, Hgb 75%. White cell count 7,900. P 71, L 27, Tr 2. Wassermann negative. Basal metabolism normal. X-ray of esophagus and stomach showed no esophageal stricture, but there was delayed gastric drainage, and a dilated duodenal bulb with a tortuous and angulated second part, suggesting adhesions. Intravenous injection of tetra-iodophenol-thalein salts fol-





toward the nose giving a hysterical appearance. The mood of the patient seems to be changing constantly. It is difficult to hold the patient's attention for even a very short time. Intelligence and orientation fair. Memory for recent events is poor. Periods of drowsiness alternate with periods of restlessness. The patient dreams much, particularly pertaining to her family relationship, she states that she has visions while she is "half-awake" of angels coming after her, she says her mother (long dead) talks to her almost constantly. The speech is drawing, articulation is fair.

All the cranial nerves are normal except for diminished sense of smell and taste. Fundi normal.

**Motor System** Some atrophy and moderate flaccidity of all muscles of forearm and carpa interossei. Motor power is markedly decreased, particularly on right arm and hand, there is no evidence of paralysis in the upper extremities, the change is principally a weakness or loss of power, or strength. There is present a fair amount of ataxia in the arms, lower extremities are too weak and painful to permit performance of tests, though there is apparently a lower motor neuron paralysis of both lower extremities with contractures of the muscles in flexion.

**Reflexes** The deep tendon reflexes of jaw, elbow and forearm are present and slightly diminished. Those of lower extremities can not be elicited because of pain.

The superficial of corneal and pharyngeal reflexes are normal. Those of abdomen not present. There is vesical and rectal incontinence. The skin suggests atrophic changes. There is pitting edema of the feet.

**Sensory System** Hyperesthesia over soles of feet. Diminished sensation of pain and touch in both forearms. Disturbed sensation of pain and touch in both legs to knees. Hyperesthesia of palms. Disturbed appreciation of hot and cold below 5th rib. (This is inconstant.)

The patient continued to grow constantly worse and finally developed hypostatic pneumonia and died, July 4th, 1928.

The Clinical Diagnosis was

Plumbism.

Posterior Root Radiculitis  
Myositis  
Hypostatic Pneumonia  
Aortitis  
Chronic Interstitial Nephritis  
Cystitis  
Atrophy of the organs of reproduction

#### AUTOPSY REPORT

Drs P Brindley and C B Sanders

The body is that of an elderly white woman about fifty years of age. The body is embalmed and rigor mortis is present. The pupils are dilated and equal. There is sordes about the mouth and the gums show a bluish stain along their margins about the teeth.

There is marked emaciation of the entire body especially of the legs and arms. There are contractures of the legs and arms and they cannot be straightened out. There is rather marked edema of the feet and legs so that they pit on pressure. There are bed sores over the buttocks. On the anterior abdominal wall to the right of the mid-line and extending up from the umbilicus there is a scar about 15 cm long. Dense fibrous adhesions are present between the under surface of the liver and the transverse colon. There is absence of the gall bladder and appendix. Rather dense fibrous adhesions between the capsule of the liver and the surrounding structures.

**Heart** Gross Weight 200 grams. The right side shows a slight amount of dilatation. All of the chambers are filled with post mortem clots. The mitral and aortic valves show a slight thickening of their margins. There are several raised yellowish patches in the first part of the aorta. Microscopic. some of the muscle fibers appear

larger than normal and show large nuclei, but many of the fibers are of normal size or smaller than normal. There is apparently a slight increase over the normal of the golden yellow pigment found at the poles of the nuclei. A slight overgrowth of connective tissue is present.

*Lungs* There are a few petechial and ecchymotic hemorrhages beneath the pleura of the left lung. The posterior portion is of a dark red color and on cut section shows an excess of blood tinged fluid. There are several areas in the lung which show a decrease in crepitus. The right lung is similar to the left and in addition shows, on cut section, multiple areas of consolidation which stand out above the neighboring cut surface. There are several small greyish nodules in the upper lobe which look like healed tubercles. There is a small dark red wedged-shaped area in the lower margin of the upper lobe. The mediastinal nodes show greyish areas of caseation and also a large amount of coal pigment. Microscopic the vessels are filled with blood. Some of the bronchi contain many polymorphonuclears and desquamated epithelium. Neighboring alveoli also contain a similar inflammatory exudate while many of the alveoli still further away from the bronchi are partly or completely filled with a serous fluid intermixed with fibrin and red blood cells. A few pigmented cardiac failure cells are present. The mediastinal nodes contain black granules of pigment, apparently coal pigment. There is also a definitely walled off partially healed conglomerate tubercle.

*Spleen* Gross weight 338 grams. On section there is an excess of blood and fibrous tissue. The pulp is soft and can easily be scraped away by the knife. Microscopic there is a rather marked excess of blood. The pulp is increased in amount and there is a marked amount of yellowish brown pigment both within the phagocytic cells and between them. The central splenic arteries are thickened and fibrosed with hyalinization of the fibrous tissue. There is fibrous tissue over-growth with hyalinization in the trabeculae.

*Liver* Gross weight 1,700 grams. The liver has rounded edges. On cut section there is an excess of blood and the liver has a mottled nutmeg appearance. Microscopic in scattered areas the liver cells show a fatty infiltration.

*Kidneys* Gross weight 200 grams. The capsule strips with difficulty leaving a roughly and finely granular surface with several subcortical cysts present which are about 10 mm in diameter. On cut section there is a slight thinning of the cortex. The right kidney is similar to the left. Weight 200 grams. Microscopic the vessels are distended with blood. Some of the glomeruli show enlargement. Congestion of the glomerular vessels, and swelling of the endothelial cells. The tubules, especially the loops of Henle and collecting tubules, show degeneration, desquamation and some necrosis. Some increase in interstitial tissue is seen especially in the cortex. Adrenals show nothing unusual.

*Pancreas* Gross shows nothing unusual. Microscopic there is an increase in fibrous tissue in the walls.

of the ducts. The vessels are distended with blood

*Genito-Urinary System.* Gross: the bladder contains about 50 cc of a turbid urine. The mucosa is congested and shows many petechial and ecchymotic hemorrhages. There is a deposit of a muco-purulent exudate on the mucous membrane.

*The Uterus* Gross is smaller than normal and the walls are atrophic and fibrosed. The ovaries are small and fibrotic. Microscopic the uterine muscle is atrophied and there is an increase in fibrous connective tissue. The glands are atrophic. There are many lymphocytes in the endometrium and a less number in the myometrium.

*Gastro-Intestinal System* Gross the stomach contains a small amount of mucus and food. There are many petechial and ecchymotic hemorrhages in the mucosa. The rectum contains dark black fecal material. There are some petechial and ecchymotic hemorrhages in the mucosa of the colon and small intestine. An excessive amount of mucus is present in the colon. There are also a few small ulcers in the colon. Microscopic: small hemorrhages are seen in the mucosa, and in areas we find absence of superficial portions of mucous membrane.

*Central Nervous System \** Gross the brain and cord show nothing unusual grossly. Microscopic: different sections of central nervous tissue, posterior root ganglia and peripheral nerves were stained with Harris' hematoxylin and phloxine, Heiden-

hain's iron hematoxylin, and Weigert's myelin sheath stain.

The brain showed nothing unusual.

The spinal cord showed many of the anterior horn cells atrophied and degenerated with a faint yellowish rather diffuse pigmentation that in some instances completely replaces the faded nucleus. Certain ganglion cells in the nucleus dorsalis showed slight evidence of degeneration. The posterior root ganglion cells contained a large amount of yellowish brown definitely granular pigment arranged perinuclearly. The ganglion cells otherwise stained well.

The peripheral nerves showed nothing unusual.

*Anatomical Diagnosis* Atheroma of the aorta, Chronic mitral and aortic valvulitis, Chronic fibrous pleurisy, Hypostatic congestion and pneumonia, Hypostatic congestion, Tuberculous lymphadenitis, Chronic interstitial splenitis, Chronic glomerulo-nephritis, Atrophy of the uterus, tubes and ovaries, Petechial and ecchymotic hemorrhages of mucous and serous membranes, Hemorrhagic cystitis, Surgical absence of the gall bladder and appendix.

#### *Microscopic Diagnosis*

*Heart* slight hypertrophy, with beginning later atrophy.

*Lungs* hypostatic, lobular pneumonia, tuberculosis of hilus nodes. Anthracotic pigmentation of nodes.

*Spleen* congestion, increased pigment, with a slight chronic interstitial splenitis.

*Liver:* fatty infiltration, slight

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## Editorial

### *Dessicated Stomach in the Treatment of Pernicious Anemia*

Following Castle's demonstration that the stomach of normal individuals secreted a substance which could develop a blood-maturing principle from meat, Sturgis, Isaacs and Sharp began experiments to determine the nature of the material in the stomach which could produce a hematopoietically active substance. Sharp, on the basis of an original theory, decided that the feeding of stomach should have the same effect on patients with pernicious anemia as liver. A preparation was made by dessicating fresh whole hog stomach and defatting with petroleum benzine, so that 30 gm of the final material represented 218 gm of the fresh tissue. This preparation has very little odor, and practically no taste. Daily feedings of from 15 to 30 gm of this preparation in suspension in water were given to three consecutive patients with typical pernicious anemia. One of these patients, a man, aged 57 years, had been treated with a preparation of liver extract about two years previously, receiving about 6 vials daily, representing the extract from 600 gm of fresh liver. At that time his initial red blood cell count varied between 800,000 and 1,000,000 per cubic millimeter, and his maximum reticulocyte count was 16 per cent on the tenth day of treatment. He developed a complete remission, but later had

a complete relapse after discontinuing the treatment. With an initial red cell count of 1,200,000 per cubic millimeter and a hemoglobin of 29 per cent, he was placed on 30 gm of dried hog's stomach, with a resultant maximum rise of 188 per cent of reticulocytes on the seventh day. He was fed 30 gm daily of dessicated whole stomach from the first to the twentieth day, from then on he was given 15 gm of the substance daily. No hydrochloric acid was given. Daily counts of the reticulocytes after the twenty-fourth day showed a variation of from 0.1 to 1.1 per cent. On the forty-sixth day the red blood cell count had risen to 4,430,000 per cubic millimeter, the hemoglobin to 76 per cent. The white blood cells had risen from 2,400 to 5,400 per cubic millimeter, and the patient showed a marked subjective and objective improvement, which began early in the course of the treatment. The second patient was under observation for fourteen days only. Given the same treatment of 30 gm dried hog's stomach daily, at the end of twelve days, his red cell count and hemoglobin had risen, the patient felt greatly improved and left the hospital. The third case was a man, age 26 years, with an initial red blood cell count of 1,470,000 per cubic millimeter, a white blood cell count of 7,500 and a hemoglobin of 35 per cent, who was given 30 gm daily of the dried stom-

ach which had been defatted with petroleum benzin. In addition the patient received 4 cc of dilute hydrochloric acid in 250 cc of water with each meal, but this was not taken at the same hours that the dessicated stomach was given. There was a very rapid and remarkable improvement similar to that observed in patients with pernicious anemia following the use of liver. In nineteen days the red blood cell count rose to 3,240,000 per cubic millimeter, the white blood cells were 4,300 per cubic millimeter, and the hemoglobin 60 per cent. In all three of these cases no liver or liver extract had been given for two months or longer before the treatment with dried stomach had begun. From the well known occurrence of spontaneous complete remissions in the course of pernicious anemia, with return of blood to normal condition and the conversion of a megaloblastic marrow into a normocytic marrow, these cases are all too insufficient evidence upon which to base as yet unqualified statements as to the value of dessicated stomach feeding, and as to whether it will replace the use of liver and liver extract. This new treatment must be tried out on a sufficiently large number of cases in order to exclude the possibility of spontaneous absolute remissions so characteristic of pernicious anemia. Should it be proved by further investigations that the remissions are not spontaneous, but are due to the use of dessicated hog's stomach, a great advance in the treatment of pernicious anemia will have been made. Tasteless and practically odorless, the new preparation will have a great advantage over the use of liver and liver extract, and the

treatment should be much less expensive than that with liver. Hogs' stomachs are, we believe, of not much commercial value at the present time, representing practically waste material. The process of dessication and defatting will add but little to the cost of the preparation, so it is to be hoped that further investigation as to the remission-provoking power of the dried hog's stomach product will be as successful as these three preliminary observations promise it to be. If the hog's stomach be shown to contain an active hematopoietic substance, as apparently do liver and kidney, it is interesting to speculate with the idea that pernicious anemia patients have lost, or have never had, the ability to secrete within their stomachs a substance which has the power to produce a blood-maturing material from food. The question also arises as to what other tissues may contain the same principle. If the hog's stomach, why not the hog's intestine?

#### *Eleventh Decennial Pharmacopoeial Convention*

This Convention for the revision of the Pharmacopoeia of the United States has been called for May 13, 1930 in Washington, D. C. All delegates must register at least sixty days before the Convention, the latest date for such registration being set at March 14, 1930. As is always the case when the time for a new Pharmacopoeia approaches there is more or less discussion as to the extent of the present day use of deleted pharmacopoeia drugs. A number of efforts have been made in the past to secure exact facts upon which to base

correct judgments for the U S P. Scope, and the Committee on Revision is again issuing an appeal for help in making such a study. To accomplish this end they have issued a questionnaire, which has been suggested by various physicians of the Committee, as a check upon the decisions of the past twenty years as to what products which were official in the Eighth or Ninth Revisions, but were not admitted to the U S P X, are in professional demand, and what is the extent of this demand. Physicians and pharmacists are earnestly invited to cooperate in this survey. There follows a long list of the medicinal products which were official in the Eighth and Ninth Revisions but were omitted from the Tenth. Physicians are asked to mark "O," indicating "Often," "R" indicating "Rarely" or "N" meaning "Never," after each of the items listed, to indicate the personal use of the item in their practice. Pharmacists are first asked the number of times the products listed have been ordered on the last 300 prescriptions they have filled. While 300 prescriptions are mentioned

as the minimum number to examine, it is urged, that whenever possible, this number be increased to 500 or 1000, or even more. But the number examined must be clearly indicated, and these must be in sequence, filed, and must be of the current year, 1929. Secondly, pharmacists are asked to indicate if any of these items have been called for over the counter by laymen, during the year, 1929, and, if possible, how often. There is also space for additions, in which the physician is asked to insert the titles of such therapeutic agents of the "newer *materia medica*" that he would recommend for inclusion in the next Pharmacopoeia. Copies of this questionnaire will be sent to any one who is interested on addressing E. Fullerton Cook, Chairman of Revision, United States Pharmacopoeia, Tenth, 636 South Franklin Square, Philadelphia. These questionnaires are to be returned before December 31st, 1929. It is desirable that physicians interested in the revision of the Pharmacopoeia should assist the Committee in furnishing such facts as are above requested.



## Abstracts

*Death During Remission Stage of Pernicious Anemia* By I ZADEK (Klin Wochenschrift, August 13, 1929, p 1527)

That pernicious anemia is a chronic disease characterized by striking spontaneous remissions and recidives has long been recognized. During such remissions it has been frequently observed that the blood picture may return to normal or approximately so, the hyperchromatic megalocytosis characteristic of the disease may disappear wholly. Since the introduction of the liver-treatment such periods of improvement occur much more frequently than in the past, during which the hematologic examination shows none of the blood changes characteristic of pernicious anemia. When a patient is examined during such a stage of remission the diagnosis of pernicious anemia by means of the blood examination is not possible. Only the presence of the accompanying clinical symptoms of achylia gastrica, funicular myelitis, myocardial degeneration and glossitis, which are not affected by the liver-treatment, will lead to the suspicion of a remission-stage of the disease. The occurrence of spontaneous absolute remission stages of pernicious anemia without characteristic hyperchromatic myelocytosis was emphasized by Zadek before the discovery of the liver treatment. The brilliant results of the new therapy have fully confirmed his views as to the assumption that pernicious anemia is not a primary disease of the bone-marrow. Zadek long before the liver treatment of the disease had demonstrated the occurrence of a metaplasia of the megaloblastic bone-marrow of the fully-blown and recidive stages of the disease to the fatty marrow of the remission stages by the direct examination of marrow removed from the living patient. The earlier views assumed a megaloblastic or megalocytic regeneration for the period of remission, and a persistence of megaloblastic marrow in this period. The normocytic blood-for-

mation of the remission period must lead to a denial of this view, for it stands to reason that an orthochromatic, normocytic blood-picture, without macrocytic or megalocytic hyperchromia, without increased vital staining, and with physiologic blood-volume index must indicate a physiologic condition on the part of the blood-forming tissues. In confirmation of his views concerning the normal state of the bone-marrow during the remission period, Zadek reports the study of two cases dying during the remission period, one without liver treatment and one with it. In the bone-marrow of the first case megaloblasts were completely lacking, and normoblasts were abundant, with many erythrocytes and nests of granulocytes between the fat-areas. Megakaryocytes were present. In the second case the marrow showed abundance of erythrocytes without megalocytes, and numerous erythroblasts, predominately in the form of small normoblasts with small clumped thick nuclei. Between these there were nests of granulocytes with a striking abundance of eosinophile myelocytes, but only occasional myeloblasts. Megaloblasts were wholly absent. It is of especial interest to note that the sternal marrow of this second patient had been examined during life during the full-blown stage of the disease and that it then showed erythrocytes with slight anisocytosis and rich polychromasia, megalocytes, normoblasts, and transitional forms to macroblasts and megaloblasts. Death occurred from influenza after a year on liver diet with complete remission. Marrow taken from the sternum at the point of original puncture was cytologically wholly different from that first examined. It is interesting to note that in both of these cases dying during a remission stage of pernicious anemia the specific megaloblastic character of the bone-marrow should be wholly absent. In the case that had been treated with liver the increase in eosinophile myelocytes in the

bone-marrow corresponded to the frequently observed eosinophilia of the remissions due to liver treatment. Since it may be assumed that cases of death through intercurrent diseases during absolute remission periods of pernicious anemia due to liver treatment will more frequently come to autopsy, it is highly desirable that they be studied for further information as to the nature of the remission and of the relationship between hemolysis and regeneration. Zadek believes that it is highly desirable that a thorough microscopic analysis of the organ changes (anadenia ventriculi, funicular myelitis, papillitis and atrophica linguae, haemosiderosis hepatis, myo-degeneratio cordis, etc.) accompanying the full-blown stage and the recidives should be carried out in the stage of absolute remission for the determination of a possible improvement of these conditions through the liver diet. It would be of great interest to determine through exact investigations whether, and to what extent, the individual organic complications of pernicious anemia are reversible in the period of absolute remission.

*Constitutional Infantile (Pernicious-like) Anemia* By E. UEHLINGER (Klin Wochenschr, August 6, 1929)

The author reports a case of infantile, constitutional anemia, pernicious in character, occurring in a boy of 6 years. The cause of the anemia was regarded as the result of a quantitative underdevelopment of the red bone-marrow, without change of bony structure. The blood-forming marrow present was completely capable of functioning, but its total mass was greatly reduced. This red blood cell-forming marrow was limited to the shaft and upper diaphysis of the femur, and to small islands in the vertebrae. All other marrow spaces were filled with fatty tissue only (lipomatosis ex vacuo). The bony substance was neither increased nor lessened in amount. There was no increase in hemolysis. The result of the hypoplastic marrow is a high grade anemia and leukopenia, and a diminution in the number of blood-platelets. When their number falls below 45,000 hemorrhagic diathesis appears as the first symptom, this intensifies the anemia. The marrow present attempts to cover the loss through re-

generation, but because of its small mass is unable to do so. There is an intense post hemorrhagic regeneration, which leads to anisocytosis, poikilocytosis, polychromasia and macrocytosis. The iron set free through blood destruction is made use of in the regeneration, so that the hemosiderosis of the spleen, liver and bone-marrow is very slight. The thrombocyte count falls quickly because of the repeated hemorrhages and insufficient regeneration. The hemorrhagic diathesis becomes more general, and increases to a final fatal hemorrhage. This case presented multiple malformations in various years, absence of left thumb, hypoplasia of left thumb, absence of right kidney, abnormal left kidney, aplasia of right seminal vesicle and right-sided genitalia, rudimentary appendix, incomplete lung lobulation and bristly hair. This multiplicity of malformations speaks for a vitium primae formationis. This disturbance occurred during the period of organ-development, since the single tissues were functionally capable. This form of anemia may be familial. The clinical picture is predominated by the hemorrhages in skin and mucous membranes resulting from the thrombopenia due to the poverty of blood. From pernicious anemia the condition is differentiated by the absence of remissions, megaloblasts and urobilinogenuria, and by the age. Pernicious anemia under 10 years is extremely rare. From splenic anemia it is differentiated by the normal-sized spleen and liver, the leukopenia and the age, from hemophilia by the normal coagulation time, and from hemolytic anemia by the normal spleen, normal resistance of the red blood cells and the lack of increased hemolysis. Both this form of constitutional, infantile anemia and the essential thrombopenia of Frank begin with a hemorrhagic diathesis. In the infantile anemia the bone-marrow damage is not limited to the megakaryocytes, but in the later stages of the disease attacks the whole erythropoietic system, and leads to a marked change in the red cell picture, which may be so marked that megalocytes and megaloblasts may appear. In the case described by Uehlinger the changes in the hypoplastic bone-marrow were limited to those of a marked regen-

erative erythropoiesis with the output into the circulation of anisocytotic and basophile granulocytes. From the differential points given above, it would seem clear that in the infantile, pernicious-like anemia there is a well-defined clinical picture.

*Zur Frage der Schutzstoffe bei Syphilis*  
By A. HAUPTMANN and A. GALLINEK  
(Klin. Wochenschr., August 6, 1929, page 1485)

Cohn had previously published the results of his work on the occurrence of protective bodies in experimental syphilis, in which he found that a spirocheticidal action of the sera of syphilitic rabbits resulted after the third injection of spirochetes. The sera of human syphilitics in different stages of the disease showed no such effects. On the other hand the serum of paretics, who had been treated with injections of dead spirochetes showed the same effect as the sera of syphilitic rabbits. The work of Hauptmann and Gallinek paralleled that of Cohn only in part, for Cohn worked with experimental syphilis and concluded that immune bodies were found only in that form. Hauptmann and Gallinek found evidence of their formation in human syphilis. These investigators worked with spirochetes derived from the Truffi-rabbit chancre. The phagocytes used were obtained from artificial exudates in the abdominal cavity of rabbits according to the method of Hamburg. The human sera used were only employed in wholly fresh condition, and only the active sera of untreated cases were made use of. The microscope was built into a Nuttall thermostat, so that a constant temperature of 37-38° was maintained. The dark field lamp was used for only short periods, in order to avoid temperature changes. Observations were made partly in ringed preparations and partly in hanging drops on liquid paraffin. The movement characteristic of spirochetes appears to be a pendulum movement which in reality is a rotation. In addition to this pendulum effect there occurs the knicking or bending motion. In the middle of the organism there will occur suddenly a knicking, the organism will either immediately straighten out again or will remain knicked for some time. Whether this knicking is, as Oelze

assumes, the sign of a beginning disintegration, is regarded as doubtful by Hauptmann and Gallinek, since they observed it to occur very early in spirochetes which were under observation for many hours before movement ceased. They also had very frequently the impression of locomotion of the spirochetes, in contrast to Oelze's view that such a spirochete movement did not occur. This apparent locomotion was the first movement to cease, so that its cessation may be regarded as an expression of least damaged vitality on the part of the organism. Actual phagocytosis of the spirochetes by the phagocytic cells was never observed, although the authors describe many interesting phenomena suggesting its occurrence. No evidence of agglutination was seen. The lowering of vitality showed itself first in the cessation of locomotion, then the pendulum motion became weaker, and finally ceased. The spirochetes then presented a stiffened appearance and finally they fragmented into a droplet-like row. Expressed in different grades of strength of vitality, the first grade would be that characterized by locomotion, strong pendulum movement, the knicking motion, and the affinity for the cells (as shown by anchoring, tangential position, star-formation and bridging between two cells). The second degree would be shown by a moderate pendulum movement as the only form of motion shown by the organism, while the third degree of vitality would be the loss of pendulum motion and beginning stiffening. Finally, the fourth stage would show itself in complete stiffening and fragmentation, which would represent its complete death. Their experiments were carried out in ten series in which the action of normal sera, with and without phagocytes, was compared with that of luetic and metaluetic sera, with and without the addition of phagocytes, on spirochetes of the same source or origin, on the same day and under the same conditions. Ten normal cases, ten secondary syphilitics, eleven cases of paresis and two cases of cerebrospinal lues were so studied. In all cases, except in the two of cerebrospinal lues the spirochetes employed were obtained from the Truffi-rabbit chancre. In all of these expe-

riments no difference was observed in the action of the serum as far as the presence or absence of phagocytes was concerned. In most of the normal sera the degeneration phenomena on the part of the spirochetes began after three hours, and were completed after five hours. In half of the secondary-syphilitic sera the beginning of the degenerative phenomena occurred in ten minutes and death of the spirochetes was complete after thirty minutes. In the other half of the sera from secondary syphilitic cases the death-phenomena began after one and a half hours and were completed after one and a half to two hours. Only in one case was the two hour period observed. Investigation of this case, which has been believed to have been untreated, showed that the patient before entering the clinic had already had 2 gm of neosalvarsan and numerous bismuth injections. The sera from the cases of paretics behaved in the same manner as the normal sera. In the two cases of cerebral syphilis, the appearance of death-phenomena took place extremely quickly. In these two cases the spirochetes used were taken from a culture. Only in these two sera was any difference shown between the phagocyte-containing and the phagocyte-free sera. In the latter the spirochetes remained unaltered essentially longer than in the sera containing phagocytes. It would appear from this that the spirochetes obtained from culture were more susceptible to cell action than those obtained from the animal body. Hauptmann and Gallnek's investigations, therefore, agree with those of Cohn, in that the sera of normal cases and of paretics contain no immune bodies. This confirms the view of Hauptmann as to the immunity-weakness of the paretic organism. On the other hand the work of Cohn which shows that paretics treated with killed cultures of spirochetes produce immune-bodies would seem to contradict Hauptmann's views, but the latter does not hold anything in Cohn's result to contradict his view of an insufficient defence on the part of the metaluetic organism, instead of an immunity-weakness, which is more of a constitutional conception, but which can also take place in that a less virulent spirochete race may excite in an organism capable of defence, a less active defence

response. In effect this amounts to the same thing as when a constitutionally defence-weak organism cannot produce sufficient defence against a highly virulent spirochete race. Hauptmann's theory of a less virulent spirochete race as the cause of metalues is only a modern expression of the old theory of "lues nervosa." If the Cohn finding of the formation of immune-bodies in paretics treated with cultures of spirochetes and the absence of such bodies in untreated cases be confirmed, the "insufficient defence" of the metaluetic in Hauptmann's theory may be taken to mean an insufficient stimulation on the part of the weakly virulent spirochete race. Before this question can be wholly decided, further investigations must be carried out to show whether the cultures of spirochetes used by Cohn are more virulent when inoculated into rabbits than are spirochetes cultivated from animals, and, further, whether the immune-body production towards these culture spirochetes is stronger in secondary syphilitics than in paretics. If this be the case, Hauptmann's conception of the constitutional weakness in defence of the paretic is confirmed. All defence on the part of the paretic organism is not wanting, it is present in part, as the occasional presence of gummatous formations in the paretic brain shows, and the occurrence of skin manifestations in the secondary stage of the paretic. If the work of Hauptmann and Gallnek be confirmed that the secondary syphilitic and the brain syphilitic in the secondary stage produce immune-bodies, while paretics do not produce such, it must be granted that one of the essential components of paralysis is a defective defence. Whether this defective defence is a constitutional weakness or whether an insufficient stimulation of a weakly virulent spirochete is the cause must be left for future investigations to determine. In conclusion, there are present in the serum of secondary syphilitics and tertiary brain syphilitics immune-bodies, in paretics none are present in the serum, or, if present, only in small amounts, as in the serum of normal cases. In paresis this insufficient defence on the part of the organism plays an important role, whether due to constitution or to a weakly virulent organism remains to be decided.

## Reviews

*Tularemia History, Pathology, Diagnosis and Treatment* By WALTER M. SIMPSON, M.S., M.D., F.A.C.P., Director of the Diagnostic Laboratories, Miami Valley Hospital, Dayton, Ohio, Formerly Senior Instructor in Pathology, University of Michigan. Foreword by EDWARD FRANCIS, Surgeon, United States Public Health Service. 178 pages, 53 text illustrations and 2 colored plates. With complete bibliography. Paul B. Hoeber, Inc., New York, 1929. Price in cloth, \$5.00.

This book is fortunate in appearing at the psychologic moment. Regarded as a rare disease in 1924, during the last five years, Tularemia has been shown to have a world-wide distribution, and to be of such frequent occurrence in man as to assume a position of distinct clinical importance. The history of this disease has been spectacular in the extreme. From its discovery in a California ground squirrel by McCoy, in 1910, up to the present time over 800 cases have been reported in the District of Columbia and in every state of the Union, with the exception of New England, Delaware and Washington, and over 1000 cases have recently been observed in man in Japan and a smaller number of cases in Japan. It has been shown to be widely distributed in nature in a great variety of animal hosts, occurring chiefly in an infectious bacteriemia of rodents due to the *Bacterium tularensis*, particularly in wild rabbits, from which it is commonly transmitted to man through direct contact with the tissue or body fluids of the infected animal, or through indirect transmission from animal to man by means of certain ticks or flies. Besides the wild rabbit the infection has been found to exist in nature among sheep, muskrats, opossums, water rats, ground squirrels, wild mice, wood-chucks, ruffed grouse, and quail. In man the infection has been frequently confused with influenza, typhoid fever and streptococcus infections. There has been a mortality of nearly 4 per cent, in other cases there has been a very slow convalescence with the development of chronic suppurative or granulomatous lesions, associated frequently with marked prostration and debility. The incubation period varies from one day to one week. The onset is sudden, frequently grippelike in character. Four distinct clinical types exist, the ulceroglandular, the oculoglandular, the glandular, and the typhoid type. The prolonged convalescence is one of the most serious features of the disease. The microscopic picture of the primary lesion is that of a subacute infective granuloma. The lesions are found chiefly in the regional lymphnodes, spleen, liver and lungs. Foci of caseous necrosis occur in these organs with peripheral epithelioid and fibroblastic proliferations. Because of the histologic similarity in the lesions of tularemia and tuberculosis there is danger in confusing the lesions. Pathologically the lesions of tularemia are to be classed with the infective granulomas. One of the remarkable features of the disease has been its frequent occurrence among laboratory workers. The diagnosis of tularemia can be easily made by an agglutination test, and there should be no excuse in the future for failure to recognize this disease. Dr. Simpson's part in the history of tularemia has also been as spectacular as the rise of the disease from comparative obscurity to its present prominence. During a period of one and a half years he discovered 61 cases in and about Dayton, Ohio. Thirty-two of the patients had acquired the disease during the rabbit season of 1927 and 1928, the remainder had suffered from unrecognized tularemia at some time during the previous twenty years. It was his Dayton experience that forms the foundation matter of the present book, which is abundantly il-

lustrated by material taken from this experience. The whole story of tularæmia from its beginning to the present time is clearly and concisely told in this book. While based primarily upon his personal experience, the book includes an excellent summary of all our present knowledge upon the subject, brought fully up to date, and including a full bibliography of the subject. This work will undoubtedly become a classic upon the subject. First in the field, it achieves merit for its completeness and logical arrangement, conciseness of treatment, with all of the important facts included, and nothing omitted. The book is printed in the usual excellent manner by Hoeber, and the illustrations are similarly well done. It is a necessary book for the library of the up-to-date physician.

*Rickets, Including Osteomalacia and Tetany*

By ALFRED F. HILSS, M.D., Clinical Professor of Pediatrics, University and Bellevue Medical College, New York City. 485 pages, 52 illustrations. Lea and Febiger, Philadelphia, 1929. Price in cloth, \$5.50.

The publication of a new book on rickets is justified by the fact that since 1918 a new era has been created—that of the Newer Rickets, which has made many time-honored theories in the textbooks no longer tenable. Two discoveries have contributed to the birth of this Newer Rickets, neither of which has depended in any way upon the other. The first came from the biologic laboratory, and consisted of a method of inducing rickets experimentally in animals, rendering it possible to study various aspects under conditions which are subject to exact control and modification. This technique made it possible for the first time to gauge the comparative etiologic importance of faulty hygiene and diet. The second factor, closely following the first, was the discovery that the lack of ultra-violet light or energy plays the dominant role in the causation of rickets, and that it is a specific agent for prophylaxis and cure. From the date of these discoveries rickets has been the object of intense investigation in many medical clinics and experimental laboratories. Interest in the disease was further stimulated by the discovery almost

five years ago that the ultra-violet rays can also exert their remarkable action indirectly—that they can endow certain oils and foods with antirachitic properties. Lastly it has been shown that a particular sterol—ergosterol—could be activated to a remarkable degree. This knowledge not only made available new methods of therapy, but necessitated a revision of our conception of the chemical action of these rays. For twelve years Hess and his numerous co-workers have been almost continuously engaged in investigations relating to rickets. The results of this work have been published in a large number of contributions to various periodicals. The more significant features of the work of these years have been reappraised and incorporated in the present volume. The book, begun about five years ago, has been written for the practitioner as well as for the nutrition worker. Throughout the book, results obtained experimentally in the laboratory have been weighed and appraised in the light of clinical experience. The clinic has been adjudged the final arbiter. A definite attempt has been made to avoid a break with the past, by presenting an unbroken exposition of both eras, welding them together into a homogeneous unit. To this end a short historical review has been introduced at the beginning of almost every chapter. No attempt at a complete bibliography has been made. The aim has been rather to have the bibliography selective and comprehensive. It is arranged according to chapters at the end of the book. In order to present a more complete picture, chapters on late rickets, osteomalacia and tetany have been included. Our point of view regarding these disorders has also been enlarged and clarified during the past decade. The conception of late rickets has been extended by the experiences of Germany and Austria during the post-war period, as well as by the recognition of renal and of coeliac rickets. The new technique used in elucidating rickets has also recently been applied to osteomalacia, and for the first time an opportunity has been furnished of comparing the radiographic appearances, the chemical analysis of the blood and the response to spec-

cific therapy of these two closely related disorders. During the past five years infantile tetany has also been studied intensively from the standpoint of the acid-base equilibrium, and has been rendered much more amenable to treatment through the introduction of the use of acid therapy, as well as of ultra-violet light. While realizing that our knowledge of rickets is far from complete, and that new and important aspects may be discovered in the not far distant future, particularly with regard to pathogenesis, the author considers that so much has been accomplished during the past decade, with a resultant remarkable change in our clinical and scientific points of view that the time for publication seemed fitting. The book consists of a most excellent survey of all the information available upon rickets at the present time. The historical survey of the subject is well written and of great interest. Most important of all is the full discussion of the work of the last decade on rickets and allied conditions from the new standpoints of diet and ultra-violet irradiation. This resume of the "newer rickets" makes the book of great value to the internist and worker in nutrition. The information contained in it has become a necessary part of the medical education of the present day, and the book a necessary item in the practitioner's library.

*Diseases of the Thyroid Gland* By ARTHUR E. HERTZLER, M.D., Surgeon to the Halstead Hospital. With a Chapter on Hospital Management of Goiter Patients by VICTOR E. CHESKY, M.D., Associate Surgeon to Halstead Hospital. Second Edition, Entirely Rewritten. 286 pages, 159 illustrations. C. V. Mosby Company, St. Louis, Mo., 1929. Price in cloth, \$7.50.

This new edition presents the results of a continuation of the studies contained in the previous one. The conclusions presented have been arrived at only after a constant comparison of the clinical picture, the pathology and a repeated examination of the patient in after years. The work is based upon individual experience and opinion in an isolated hospital "untrammeled by the opinion of others." The contents are divided into the following chapters: Etiology

of goiter, normal morphology, pathologic anatomy, symptomatology of diseases of the thyroid gland, diagnosis of diseases of the thyroid gland, goiters in unusual places, hospital management of goiter patients, topographic anatomy of the thyroid gland, and the technique of operations on the thyroid gland. This book presents a very superficial discussion of the etiology and pathology of goiter. The author apparently has no idea of the theory of a Graves' constitution, or of the relation of a persistent thymus to the so-called toxic forms of goiter. Nor does he evaluate the significance of the constant presence in exophthalmic goiter and the so-called toxic adenoma of hyperplastic lymph follicles with germinal centers. The book contains far too much evidence of having been written "untrammeled by the opinion of others." The illustrations are in part fair, and in part poor. The surgical sections have more practical value than the pathologic.

*Diagnostic Methods and Interpretations in Internal Medicine* By SAMUEL A. LOEWENBERG, M.D., F.A.C.P., Assistant Professor of Clinical Medicine, Jefferson Medical College, Assistant Physician to the Jefferson Hospital, Visiting Physician to the Philadelphia General Hospital, etc. 1032 pages, 547 illustrations, some in colors. F. A. Davis Company, Philadelphia, 1929. Price in cloth, \$10.00.

The author has ventured to compile a textbook of general information upon medical diagnosis from the standpoint of the rapidly disappearing general practitioner. The book aims to cover the field of diagnostics in internal medicine. It gives instructions on the various methods of examining the patient, descriptions of normal findings, enumeration of pathologic conditions with the normal and pathologic physical signs, and, whenever possible, the reasons for such signs. The signs and interpretations are discussed from the viewpoints of the medical student, the general practitioner and the specialist. The respiratory and cardiac systems are discussed fully and minutely, to the digestive system, the nervous system and urology, adequate space is devoted, while to the skin, nose, ears, eyes, bones

and joints, radiography, the blood, the ductless glands, etc, less space is given, only so much has been allotted as is deemed necessary for the purpose of a general examination. The chapter on laboratory interpretations is limited, in the main, to the interpretation of laboratory analyses by the pathologist, chemist, serologist or clinical laboratory specialist, while only the simplest technical methods are described. There are general chapters on the life insurance examination, industrial examinations and the detection of malingering. The illustrations are of three types: actual photographs of methods of examination and of patients suffering with the particular disease described in the text, drawings calculated to

emphasize the descriptions of certain conditions, and photographs of pathological specimens to aid the memorizing of the respective clinical descriptions. This book contains an immense amount of useful information. Its arrangement is good, and the material is concisely expressed. It is illustrated by a large number of pictures well adapted for showing the given condition, but which unfortunately suffer from the rather indistinct reproductions. Glazed paper has been used for the reproduction of the radiographs, and there are very much better than the illustrations given in the text. On the whole, this volume will be of service to the student of diagnosis.



## College News Notes

### 1930 CLINICAL SESSION TO BE HELD IN MINNEAPOLIS

The 1930 Annual Clinical Session of the American College of Physicians will be held in Minneapolis, Minnesota, during the week of February 10, 1930. Dr. S. Max White, 1009 Nicollet Avenue, Minneapolis, is the local General Chairman of Arrangements, and is busily engaged in the preparation of the program. The University of Minnesota Medical School and local hospitals throughout Minneapolis are cooperating in placing their laboratories and clinical facilities at the disposal of the College. The afternoon and evening scientific sessions will be held in the public Auditorium, where also will be housed the Registration Headquarters, Exhibits, etc. The Curtis Hotel, located two squares from the Auditorium, will be headquarters for the Officers, Board of Regents and Board of Governors. Ideal facilities for the Session, the hospitality of the City of Minneapolis and the enthusiasm and earnestness of those making preparations for the meeting combine to assure a most interesting and successful Clinical Session for the coming winter.

### PAPERS DELIVERED BEFORE ANNUAL CLINICAL SESSIONS OF THE COLLEGE

Scientific papers delivered before the Annual Clinical Session of the American College of Physicians become the exclusive property of the College for publication in *ANNALS OF INTERNAL MEDICINE*. It is very important, not only for sake of the Journal, but also for the members of the College at large, to have a complete published record of all papers delivered at each Clinical Session. The *ANNALS* is the official vehicle of the College for the publication of all such papers.

### 1929-30 DIRECTORY OF THE AMERICAN COLLEGE OF PHYSICIANS

During the past summer, the Executive Secretary, Mr. E. R. Loveland, completed the publication of a new and complete Directory of the College, and has distributed a copy to every member of record in good financial standing. Members with waiver of fees due to having passed the age limit may secure a copy on subscription of one dollar, fifty cents.

The new edition of the Directory was printed in accordance with the instructions of the Committee on Directory and the Board of Regents. The contents of this edition have been limited to such important biographical data as space permits in a volume of this size, and has been considered necessary and helpful for reference.

Although great effort was directed toward the elimination of errors, it is possible that some incomplete or imperfect data have appeared. Members are requested to advise the Executive Secretary of such errors in order that later corrections may be made.

### VOLUME FILES FOR ANNALS

The Executive Office at 133-135 S. 36th Street, Philadelphia, Pa., maintains a supply of box files specially made and indexed for Volume II of *ANNALS OF INTERNAL MEDICINE*. Volume II was completed with the June, 1929, Number, and should be preserved in one of these Volume Files. The cost is \$1.25, postpaid.

Dr. John H. Musser (Fellow and President) delivered the annual oration in medicine, speaking on "The Normal and the Diseased Heart," at the eighty-eighth anniversary meeting of the State Medical Society of Wisconsin at Madison during the week of September 9.

Dr J A E Eyster (Fellow), Professor of Physiology at the University of Wisconsin, is author of a new book entitled "The Clinical Aspects of Venous Pressure," recently published by The Macmillan Company of New York City

Dr George R Minot (Fellow), Boston, is Editorial Advisor of The Macmillan Company of New York City in the publication of The Macmillan Medical Monographs. The publications of The Macmillan Company are regularly announced on page 1 of the advertising section of this Journal

At the recent meeting of the California Medical Association at Coronado Beach, California, Admiral E R Stitt (Fellow), Dr W S Thayer (Fellow) and Dr John H Musser (Fellow) were three of the six speaker guests at this, the fifty-eighth annual session

Dr William A White (Fellow), Superintendent of St Elizabeth's Hospital, Washington, D C, is Chairman of the Board of Managers of the Washington Institute for Mental Hygiene

Dr Allen H Bunce (Fellow), Atlanta was elected a member of the Board of Trustees of the American Medical Association at its last meeting in Portland

Dr E C Thrash (Fellow), Atlanta, has been appointed Chairman of the Reference Committee on Constitution and By-Laws of the American Medical Association

Dr Cornelius Oliver Bailey (Fellow), Dallas, Texas, has been made a Fellow of the Royal Society of Arts, London. It is said that there are only seventeen American physicians who have been elected to this society

Dr David C Wilson (Fellow), has been appointed Associate Professor of Psychiatry and Neurology at the University of Virginia. Dr Wilson was formerly on the staff of the Chiton Springs Sanitarium, Chiton Springs, New York

Dr Bernard L Wyatt (Fellow), formerly President and Director of the Desert Sanatorium and Institute of Research, announced the opening of an office in Tucson, Arizona, on October 1. Special attention will be given to arthritis and rheumatoid conditions

Dr Donald R Ferguson (Fellow), Philadelphia, is author of an article which appeared in the August Number of the Hahnemannian Monthly, entitled, "Massive Collapse of the Lung Secondary to Bronchogenic Carcinoma"

Dr Arthur L Holland (Fellow), New York, Dr W W Herrick (Fellow), New York, and Dr George E Brown (Fellow), Rochester, Minn, were among the guest speakers at the Fifth Annual Clinical Congress of the Connecticut State Medical Society at New Haven during September

Dr Harlow Brooks (Fellow), New York, is Chairman of the Second Annual Graduate Fortnight of the New York Academy of Medicine, being held October 7-19. Among Fellows of the College offering papers or lectures are

Dr Max Einhorn  
Dr Charles A McKendree  
Dr Charles F Tenney  
Dr Joseph Lintz  
Dr Aaron S Blumgarten

Major Robert D Harden (Fellow), Medical Corps, U S Army, has been appointed a member of the National Board of Medical Examiners, succeeding Col Joseph F Siler (Fellow), who has been detailed to the Panama Canal Zone for duty

The following Fellows of the College have been appointed members of the Board of Public Health Advisers for Illinois by Governor Emmerson. Dr James H Hutton, President-Elect of the Chicago Medical Society, Dr William A Evans, former Health Commissioner of Chicago

Dr William S Baldwin (Fellow), Lorain, Ohio, was recently elected President of the Lorain County Health Council

Dr Rock Sleyster (Fellow), Wauwatosa, Wisconsin, recently addressed the Walsworth County Medical Society on "Nervous and Mental Diseases"

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At the meeting of the American College of Radiology, at Portland, Oregon, during July, Dr Rollin H Stevens (Fellow), Detroit, was elected President-Elect and Dr Albert Soiland (Fellow), Los Angeles, was re-elected Executive Secretary

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Dr Curran Pope (Associate), Louisville, was honored by a testimonial dinner at the Annual Meeting of the American Electrotherapeutic Association at Indianapolis, September 11-13

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Lt Comdr Elwood A Sharp (Fellow) has recently resigned his commission in the U S Navy

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Capt Frank L Picadwell (Fellow) has been transferred to the Receiving Ship, New York City

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Lt Comdr Eben E Smith (Fellow) has been assigned to the U S S Saratoga

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Comdr Lester L Pratt (Fellow) has been assigned to the Navy Hospital, Washington, D C

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Dr Gerald B Webb (Fellow), Colorado Springs, is the Research Director of the Colorado Foundation for Research in Tuberculosis

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Col Aaron C. Conaway (Associate), Marshalltown, Iowa, was in command of the three hundred and forty-seventh medical regiment at Fort Snelling, July 5-19

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In addition to acting as Director of the Desert Sanatorium and Institute of Research at Tucson, Arizona, Dr Allen K Krause (Fellow) will fill the appointment as Clinical Professor of Medicine at Stanford University, San Francisco

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Dr William Sydney Thayer (Fellow), Baltimore, received the honorary degree of

Doctor of Laws at the commencement of McGill University, Montreal, Canada

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Dr Carroll M Pounders (Fellow), Oklahoma City, addressed the Stephens County Medical Society at Marlow, Oklahoma, recently

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Dr Archibald N Sinclair (Fellow), Honolulu, Hawaii, was elected Secretary of the Hawaii Territorial Medical Association at its last annual meeting

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Dr Alfred Stengel (Master), Professor of Medicine at the University of Pennsylvania Medical School, member of the Medical Board of the University's Trustees and Chairman of the Building Committee delivered the principal address at the dedication of the new Martin Maloney Medical Clinic Building of the University of Pennsylvania Hospital in Philadelphia on September 20. The Clinic Building costs approximately one million dollars, and will house the general medical outpatient department of the University Hospital, dispensaries for medical and allied groups, a Hydro-therapy and Psycho-therapy Department, special wards for cases requiring special study and care, the Pepper Laboratory of Clinical Medicine and the John Musser Department of Research Medicine. In addition, the Eldridge R Johnson Foundation for Research in Medical Physics, provided for by the gift of \$800,000 by Mr Johnson, former President of the Victor Talking Machine Company, will occupy the entire sixth floor. The Cardio-Vascular, Gastro-Intestinal, Thyroid, Metabolic and Diabetic, Asthma, Pulmonary and Biometric Clinics will be located in the new building, and both the Pepper and Musser units will have approved facilities for their work

Dr Stengel, it is reported, was directly responsible, through his contacts with Mr Maloney and Mr Johnson, for securing the interest of these capitalists and their subsequent gifts to the University of Pennsylvania

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Dr Emanuel Libman (Fellow), New York, recently donated \$10,000 to Johns

Hopkins University Medical School for the establishment of a lectureship in the history of medicine. It is to be named the Hideyo Noguchi Lectureship.

Dr Walter A. Bastedo (Fellow), New York, was awarded the honorary degree of Doctor of Science at the Columbia University Commencement last June.

Dr Frank Smithies (Master), Chicago, delivered the opening address of the 1920-30 program of The Academy of Medicine at Rochester, New York, on October 2. Dr Smithies' subject was "Deficient Liver Function as a Cause of Chronic Skin Lesions."

Dr W. Blair Stewart (Fellow and Governor for New Jersey) was the representative delegate from the Medical Society of New Jersey to the annual meeting of the Medical Society of Pennsylvania at Erie, Pa., during the early part of October.

Dr James L. McCartney (Fellow), Hartford, Conn., was appointed Chief of the Division of Mental Hygiene in the Connecticut State Department of Health and began his service August 1. Dr McCartney was elected a Fellow of the College at the last session. For the last several years he has been specializing in neuro-psychiatry, and last year was with the National Committee for Mental Hygiene in New York City. He is now in charge of the Neuro-psychiatric work in the State of Connecticut.

Dr Robert M. Moore (Fellow), Indianapolis, presented a paper on "Subacute Bacterial Endocarditis—Some Clinical Observations," before the Indiana State Medical Association at Evansville, Indiana, September 26.

Dr Joseph Kopecky (Fellow), Galveston, is reported to have recently resigned the professorship of Clinical Medicine and Clinical Pathology at the University of Texas School of Medicine to go into private practice at San Antonio. Dr Kopecky recently

returned from Mexico City where he served during the summer as exchange Professor at the Mexico National University Medical School.

Dr Fred Morris Meixner (Fellow), Peoria, Ill., is the author of an article entitled, "Recognizing Tonsil Infection," appearing in the June, 1929, Issue of the Illinois Medical Journal.

"Physical Standards in Aviation" is the title of another article by Dr Meixner in the August Issue of the Bulletin of the Peoria Medical Society.

Dr W. H. Marshall (Fellow), Flint, Michigan, contributed a paper on "Drug Therapy" in a Symposium on Therapeutics given at the meeting of the Michigan State Medical Society, Jackson, Michigan, September 19.

Dr Antonio D. Young (Fellow), Oklahoma City, was recently elected Chairman of the combined Medical and Neurological section of the Oklahoma State Medical Society.

Dr Conrad Wesselhoeft (Fellow), Boston, was recently promoted to Assistant Professor of Theory and Practice at Boston University School of Medicine.

Dr A. B. Olsen (Fellow), Battle Creek, Michigan, is the author of an article, "Some Observations of the Treatment of Surgical Tuberculosis by Heliotherapy," appearing in the September Issue of the Journal of the Michigan State Medical Society. This paper was read before the last annual meeting of that Society, and was illustrated by slides showing the treatment as given by the natural sunshine and artificial light in Switzerland and in England.

At the joint meeting of the American Electrotherapeutic Association and the Western Physical Therapy Association, held at Indianapolis, Indiana, September 11-13, Dr Olsen read a paper on "Cryo-aerotherapy or Cold Air Treatment." The paper was illustrated by slides showing this treatment as given at Leysin, Switzerland, Alton Park,

England, and at the Battle Creek Sanitarium

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Dr Curran Pope (Associate), Louisville, Kentucky, was honored by a testimonial dinner given by the American Electrotherapeutic Association and the Western Association of Physical Therapy "in recognition of his honorable service of forty years as physician, neurologist, author, editor-writer, teacher, speaker and as one of the real pioneers in the domain of Physical Therapy in Medicine" at the Lincoln Hotel in Indianapolis, Indiana, on September 11

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Dr V C Rowland (Fellow), Cleveland, was recently elected trustee of the Ohio Public Health Association for a term of three years

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Dr Julius Friedenwald (Fellow), Baltimore, has been elected Chairman of the Gastro-enterological Section of the American Medical Association for the coming year

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Dr Russell C Pigford (Associate) has been appointed Head of the Department of Electrocardiography at St John's Hospital, Tulsa, Oklahoma

Dr Pigford presented a paper on "Reliable Signs of Myocardial Disease" at the July meeting of the Osage County (Oklahoma) Medical Society

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Dr Ada E Schweitzer (Fellow), Indianapolis, Indiana, supervised the conduct of the "Better Baby Demonstrations" at the Indiana State Fair during the summer 1,239 babies were examined, and 65,000 visitors who came to see the demonstrations were furnished information concerning child care, feeding and habit training. The attractive manner of presenting health education won much commendation. The American Medical Association donated 2,000 sample copies of Hygeia for distribution at the demonstration nursery. Dr Schweitzer is the Director of the Division of Infant and Child Hygiene of the Indiana State Board of Health.

Dr Aaron C Conaway (Associate), Marshalltown, Iowa, has announced an association with Dr Anatole Kolodny, Professor of General Surgery and Neurological Surgeon at the Iowa State University College of Medicine. Dr Conaway is Councillor for the Fifth District of the Iowa State Medical Society, President of the Marshall County Medical Society and President of the staff of the Deaconess Hospital

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At the meeting of the Dallas Southern Clinical Society, September 18-20, the following members of the American College of Physicians delivered papers

Dr Eugene Rosamond (Fellow), Memphis—"Enterospasm"

Dr Edgar W Loomis (Associate), Dallas—"Bilateral Phlebitis"

Dr H Leslie Moore (Fellow), Dallas—"The Overactive, Undernourished Child"

Dr J L Goforth (Fellow), Dallas—"Immunologic Diagnosis, Treatment and Prevention of Disease"

Dr D L DeBuys (Fellow), New Orleans—"Some Interesting Observations in the Newly Born"

Dr Robert M Barton (Associate), Dallas—"Classification of Heart Disease"

Dr C O Bailey (Fellow), Dallas—"Treatment of Acute Respiratory Infections with X-Ray"

Dr Tate Miller (Associate), Dallas—"Modern Management of Gastric Ulcer"

Dr Porter P Vinson (Fellow), Rochester, Minn—"Differentiation and Treatment (with special reference to Bronchoscopic Management) of Chronic Pulmonary Diseases"

Dr G E Brereton (Fellow), of Dallas, is the Treasurer of the above Society

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Dr G L Pinney (Fellow) has been made Chief of Staff of Internal Medicine at the Mary Lanning Memorial Hospital at Hastings, Nebraska

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Dr Austin B Jones (Fellow) addressed the Missouri State Medical Association at Springfield, Missouri, May 16, on "Agranulocytic Angina"

Dr Hubert Work (Fellow), founder of Woodcroft Hospital at Pueblo, has returned to Colorado and has offices with his son Dr Philip Work, in Denver. Dr Work has been in Washington for several years, serving as Postmaster General and Secretary of the Interior, and more recently as Chairman of the national Republican Committee. He was a member of the House of Delegates of the American Medical Association for several years and President of the Association in 1921.

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Dr Harold E. Robertson (Fellow), Rochester, Minn., is a speaker on the program of the fifty-ninth annual session of the Colorado State Medical Society, on "Some of the Newer Aspects of Carcinoma", Dr Earl H. Bruns (Fellow), Medical Corps, U. S. Army, will speak on "Air Embolism as a Complication in Artificial Pneumothorax Therapy", and Dr Gerald B. Webb (Fellow), Colorado Springs, will exhibit the Harvey film which was prepared by the Royal College of Physicians of London for the tercentenary of Harvey.

Dr Carl Vernon Weller (Fellow) published in the Archives of Pathology, March, 1929, the most complete survey of the Pathology of Primary Carcinoma of the Lung that has yet been made.

In the Journal of Cancer Research for October, 1929, he has an article on "Entdiferentiation in Primary Carcinoma of the Bronchi and Lungs".

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In the Journal of Cancer Research for July, 1929, Dr A. S. Warthin (Master) has an article on "Papillary Cystadenoma Lymphomatosum".

In the British Medical Journal for August 1929, Dr Warthin has an article on "Lesions of Latent Syphilis".

The American Journal of Syphilis for July, 1929, contains an article by Dr Warthin on "A Silver-starch-gelatin Method for the Demonstration of Spirochetes in Single Tissue Sections". This article will be published also in The British Journal of Venereal Diseases.

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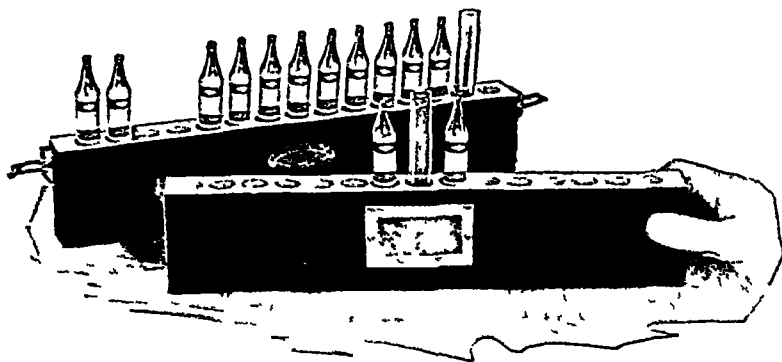
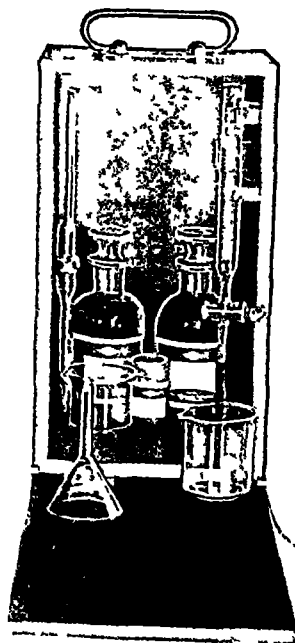
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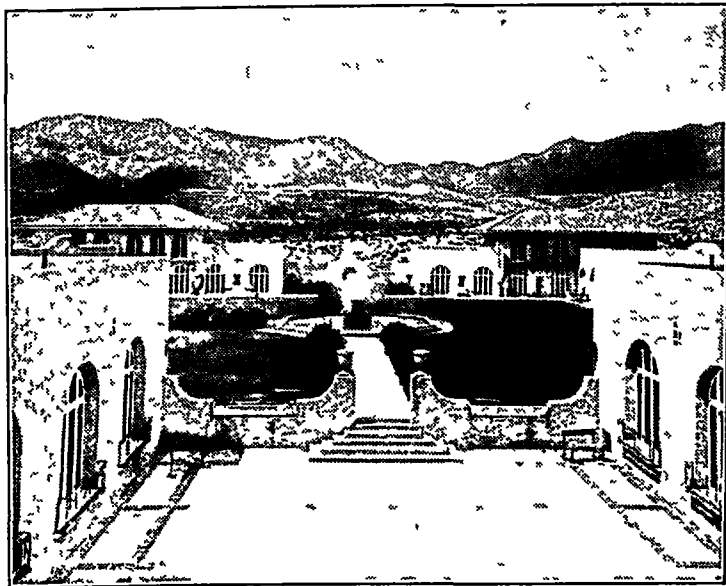
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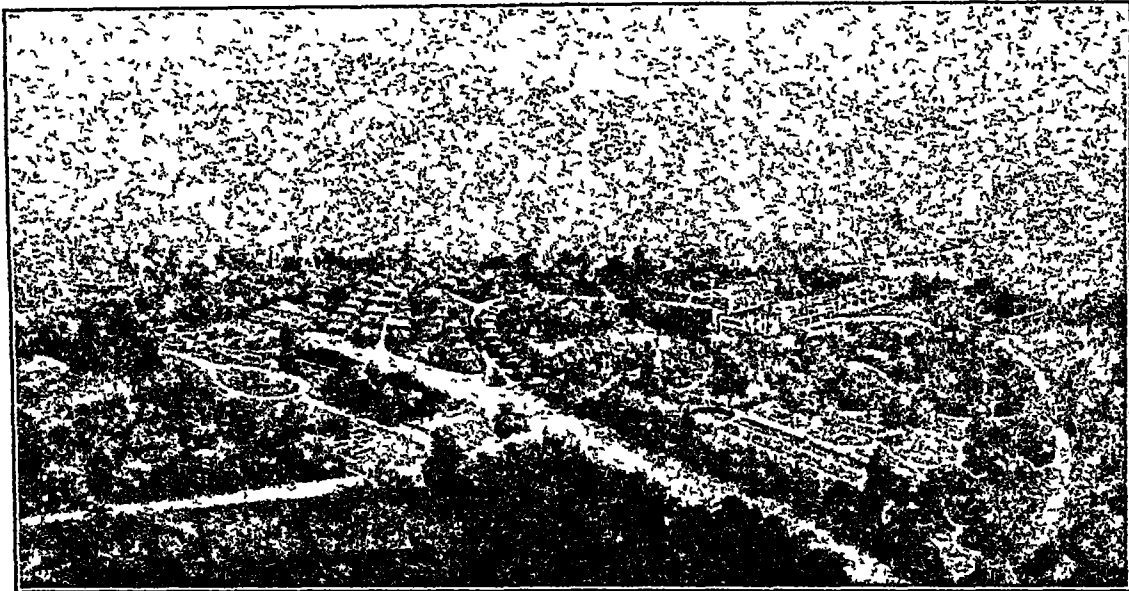
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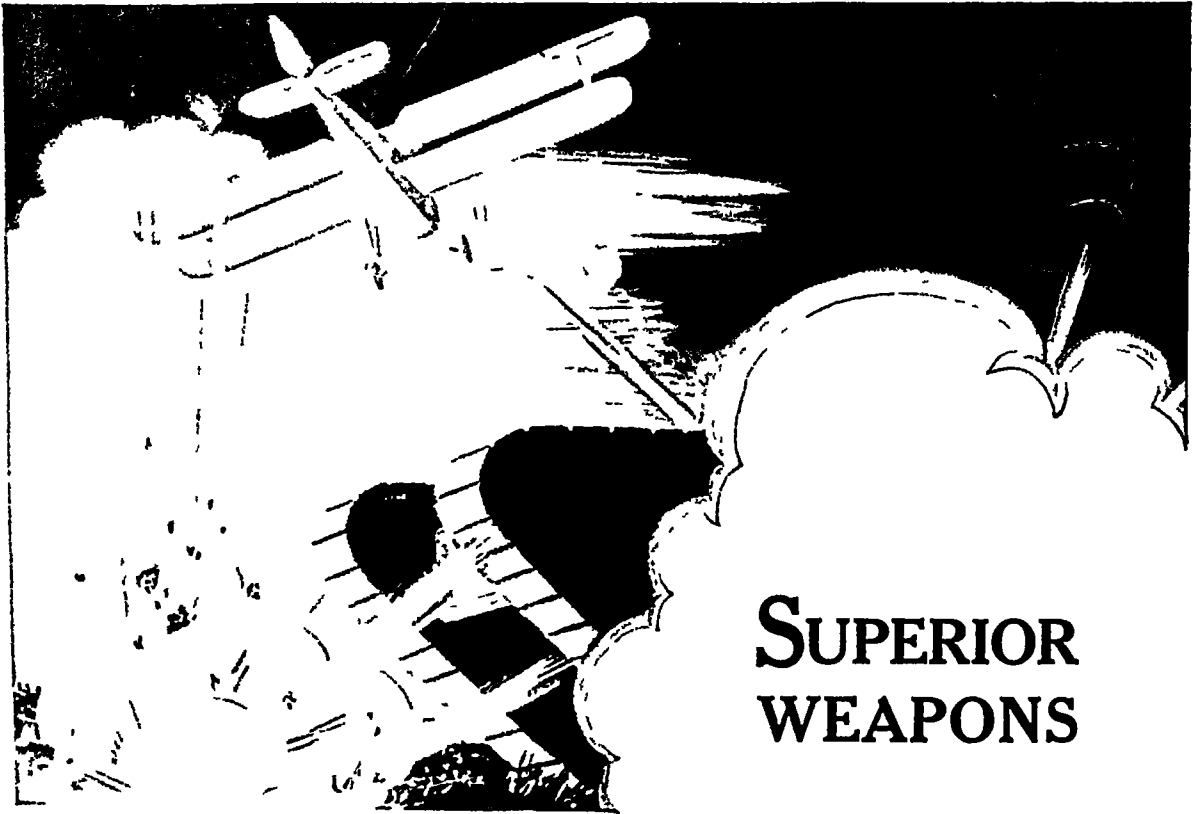
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# A Study of Intestinal Flatulence\*

By JOHN L. KANTOR, M D, and JEROME A. MARKS, M D, *New York*

## I PHYSIOLOGY OF GAS IN THE INTESTINE

**N**ORMALLY gas is present in the intestine in small amounts, insufficient to cause annoyance. It is readily passed, chiefly with the bowel movements, and is for the most part, odorless. The origin of this gas is two-fold, from the atmospheric air, and from food-stuffs.

Atmospheric air is swallowed during eating, and especially while drinking. By far the greater part of the ingested air is quickly belched. What little is left in the stomach assumes significance because it is composed of 80% nitrogen which is practically unabsorbable by the body and 20% oxygen which is absorbed in part only. This residue, accordingly, is forced to make the transit of the entire digestive tract, and appears almost quantitatively in the flatus.

Enormous quantities of gas must be produced during the intestinal phase of digestion, the exact amount and composition depending upon the diet. Inasmuch as most of this gas is readily absorbed in the blood stream, to be fixed there or exhaled through the expired air, the healthy individual re-

mains entirely unconscious of this phase of digestion. By far the greatest part of the gas produced by food digestion is carbon dioxide. This has the following sources: (1) In the upper small intestine, from a mixture of the acid gastric contents with the carbonates present in the alkaline biliary and pancreatic secretions. The amount thus manufactured has been estimated by v. Bunge<sup>7</sup> at six liters daily. (2) In the lower small intestine from the *possible* bacterial decomposition of sugars. It is to be recalled that sugars and starches are normally broken down by enzymic action to monosaccharids which are readily absorbed as such. It does not seem likely that, in health, much monosaccharid would be available for decomposition to CO<sub>2</sub> by bacterial action. At any rate no figures are available in the literature. (3) In the ceco-colon from the bacterial decomposition of cellulose, there being, in man, no enzyme capable of attacking this substance. Cellulose produces CO<sub>2</sub> and fatty acids, which in turn, liberate more CO<sub>2</sub> when neutralized by the alkaline carbonates secreted in the proximal colon.

Other gases, normally present in small amounts, are marsh gas (CH<sub>4</sub>) and hydrogen, from cellulose, and occasionally traces of indol, skatol, hy-

---

\*From the Department of Practice of Medicine, Presbyterian Hospital, and College of Physicians and Surgeons, New York City.

drogen sulfid, and ammonia, from the putrefaction of proteins. The last four gases are odoriferous,  $\text{CH}_4$  and  $\text{H}_2$  are inflammable. Carbon dioxide is by far the most readily absorbable gas, nitrogen the least, the other gases range as follows in order of their absorbability:  $\text{H}_2\text{S}$ ,  $\text{O}_2$ ,  $\text{H}_2$ ,  $\text{CH}_4$ . For details see Fig. 1.

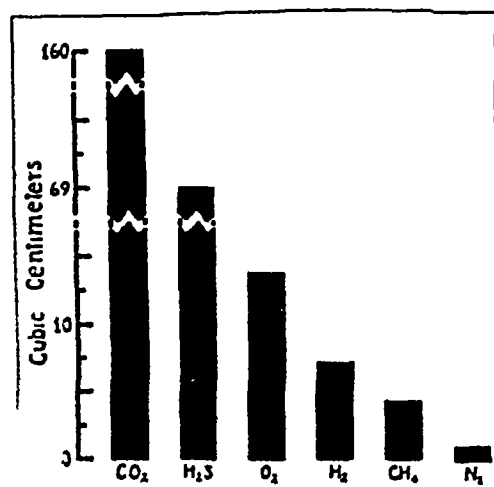


FIG. 1. Relative rates of absorption of various gases introduced into the intestine (after Melver).

Gas absorption has been shown to follow the physical laws of diffusion (Dunn and Thompson<sup>7</sup>, Melver<sup>8</sup>). It has been definitely demonstrated that the walls of the intestine are permeable to gases and that an active interchange takes place, tending to keep the gases on the two sides of the mucosa in equilibrium. A. Melver<sup>8</sup> has shown that

moment, of air admixture, gas production from food digestion, gas absorption from the intestine and possible gas diffusion into the intestine, the last named factor being probably unimportant in health. In flatus, as might be expected, it is the unabsorbable gases that predominate, as may be seen in the following analysis by Fries<sup>11</sup>:

$\text{CO}_2$	10.3	volumes per cent
$\text{O}_2$	0.7	volumes per cent
$\text{CH}_4$	29.6	volumes per cent
N	29.4	volumes per cent

Inasmuch as no nitrogen is produced during digestion, all of this gas is assumed to result either from the air originally swallowed, or from gas secreted from the blood in the process of equilibration.

The amount of gas passed per rectum is estimated at 1 liter daily (Fries). This is to be contrasted with the much greater amount absorbed. Tacke<sup>9</sup>, working with rabbits, found that ten to twenty times as much intestinal gas escapes by the lungs as by direct expulsion from the lower bowel. The figures for man are unavailable.

## II. PATHOLOGY OF GAS IN THE INTESTINE (FLATULENCE, METEORISM, ETC.)

TABLE I

Incidence of the More Common Complaints of Dyspeptics  
(Based on 2,500 histories)

SYMPTOM OR CONDITION	INCIDENCE (PER CENT)
1 Constipation	46.5
2 Abdominal Pain	46.2
3 Flatulence	33.4
4 Belching	33.1
5 Headaches	22.8
6 Vomiting	19.7
7 Epigastric Distress	13.3
8 Heartburn	10.8
9 Weight Loss	7.4
10 Diarrhea	7.1

TABLE II

Relation of Flatulence to Some Common Disorders	
INCIDENCE OF FLATULENCE	PER CENT
Chronic Stomach Bubble	70.5
Colitis	49.7
Redundant Colon	46.7
Hypertension	46.5
Diarrhea	41.0
Belching	38.6
Neurosis (all functional dyspepsias)	35.0
In unselected cases (general incidence)	33.4
Constipation	28.8
Cholecystitis	28.6

Despite a careful consideration of these factors, we found no evidence that either sex, body habitus, or gastric acidity, affected the incidence of flatulence. On the other hand certain clinical conditions shown in table II seemed to bear a definite etiologic relationship to the incidence of intestinal gas accumulations. Some of these factors will be discussed in detail later.

*Etiology*—The etiology of flatulence may be considered under the following heads:

A Excessive gas intake or production

- 1 From atmospheric air
- 2 From food decomposition
- 3 From abnormal bacterial flora (intestinal infection)
- 4 From the blood

B Deficient gas expulsion

C Deficient gas absorption

- 1 From interference with intestinal blood supply
- 2 From interference with mucosal integrity
- 3 From interference with intestinal muscular tone

A Flatulence Due to Excessive Gas Intake or Production

Ingested carbon dioxide, as in charged beverages, is either quickly belched, or rapidly absorbed, even from the stomach. It is therefore not likely to produce flatulence.

*Rôle of Atmospheric Air*—This has long been known to cause flatulence. Its rôle may be considered under the following circumstances of clinical interest.

Air is introduced into the stomach abnormally by air swallowing, air sucking and neurotic belching (Wyllie<sup>12</sup>) (Kantor<sup>13</sup>). The net result of all these procedures is an increase in the air in the stomach and secondarily in the intestine as well. The consequent degree of flatulence really depends on the relative patency to gas of the cardia in the retrograde and of the pylorus in the physiologic direction.

Thus in the "chronic stomach bubble" a condition apparently due to spasm of the cardia in the retrograde direction, gas is continually present in the stomach in large amounts as can be readily determined both by physical examination and roentgenologically (fig. 2). There being no way for the gas to escape upward, it has to go through the pylorus and flatulence results. In our series of chronic stomach bubble cases flatulence was present in 70%. Although the condition of chronic stomach bubble is not common—it occurred in 27 of 1533 x-rayed patients (1.76%)—it must be recognized when it does occur, as one of the most common causes of intestinal flatulence.

Recent analyses of intestinal gas from post-operative cases, as performed by McIver<sup>14</sup>, show that the composition of the flatus is such that it resembles air modified by interchange with the blood gases. This observer concludes that swallowed air plays an important rôle in the production of postoperative distention. Possibly other factors to be discussed later also enter into the etiology of this disorder.

Self-inflation or auto-inflation is a condition that has long intrigued the medical profession. Many observers regard it as due to air swallowing or air sucking by neurotic or hysterical subjects. It can take place quickly as in the case of the malingerer described by Magendie<sup>15</sup>, and may be relieved by gas passage either at will, or under hypnosis, as v. Noorden<sup>16</sup>, has reported. Here again, however, other factors than swallowed air must be considered.

*Rôle of Food*—Flatulence is ordinarily associated with a preponderantly vegetable diet, the degree of gas formation being in inverse proportion to the utilization of the carbohydrate. Thus such articles as white bread, fine cereals, dextrin, and sugar produce very little gas, whereas pumpernickel, the cabbage family (broccoli, brussels sprouts, cauliflower, kale, kohlrabi, sauerkraut and slaw), turnips, carrots, beets and legumes (peas, beans and lentils) are well-known causes of flatulence.

As already mentioned, pure sugars and starches are digested to the stage of monosaccharids and are absorbed as such. It is conceivable that under





FIG 2 Chronic stomach bubble Appearance 9 hours after barium meal

pathologic conditions a certain amount of further bacterial decomposition may take place, but unless some other gas than  $\text{CO}_2$  is produced not much flatulence would result.

It is the cellulose-rich vegetables, namely, those in which the starch granules are enclosed in tough cell membranes, that cause trouble. This is so because, as already stated, specific bacterial action in the ceco-colon is the only method available for the decomposition of cellulose. As a result of this action there are produced various fatty acids, such as formic, acetic, lactic, succinic, valerianic, as well as  $\text{CO}_2$ ,  $\text{H}_2$ ,  $\text{CH}_4$ , (Schmidt and v Noorden<sup>10</sup>). The amount of gas evolved is probably considerable, for Schwartz<sup>12</sup> found that if 100 grams of cellulose were completely decomposed at  $38^\circ \text{C}$ , they would yield

$\text{CO}_2$	19.5 liters
$\text{CH}_4$	7.5 liters
$\text{H}_2$	4.0 liters

or 31 liters of gas in all. It need hardly be pointed out, however, that, as everyone knows from stool examinations, the digestion of cellulose is never complete in man.

Furthermore certain vegetables such as cabbage, radishes, onions and garlic contain allyl sulfid and allyl mustard oil. Even while cooking they split off certain odorous and possibly toxic gases such as hydrogen sulfid and methyl mercaptan.

suffering from colitis, the ingestion of raw whole milk is associated with an annoying flatulence. This was found by Ruge<sup>20</sup> to be due to hydrogen, presumably from the milk protein. McIver found 33% of this gas in the flatus of patients on a milk diet.

If there is much delay in the colonic transit of proteins, stinking gases such as skatol and indol may be produced. It should be borne in mind that certain of the odorous gases are capable of absorption into the blood and of excretion through the expired air. Thus, for example,  $\text{H}_2\text{S}$  is 4 to 5 times as absorbable as  $\text{O}_2$  (see fig. 1), and according to some (Lauder Brunton)<sup>6</sup>, the former gas may actually appear in the expired air. Since this phenomenon obviously furnishes the physical basis for halitosis it would be extremely interesting to secure exact information as to what gases are responsible for the odor of the breath in this condition. Unfortunately no such studies appear to have been made as far as we can learn. That most of the fetid intestinal gases are probably deodorized during their passage through the liver is pointed out by Alvarez who found that as long as an experimental rabbit is kept alive, the bowel gives off no odor and the breath is not offensive, but that as soon as the animal is dead, the stench from the cecum becomes annoying. This is in line with an early observation of Hertter and Wakenhut<sup>21</sup>, that the hepatic, renal, and intestinal epithelial cells have the power of absorbing considerable quantities of indol and of combining it locally in such a way that this substance cannot be recovered by distillation. It is interesting to spec-

ulate whether some of the heavy breath of liver insufficiency may not possibly be due to the failure of hepatic deodorization of odorous intestinal gases

Clinically, putrid intestinal gases are often associated with alcoholic dyspepsias (note the breath) as well as with the decomposition of protein-containing exudate in cases of severe catarrhal or organic disease of the intestine (Strassburger)<sup>24</sup> In general, the expulsion of foul flatus suggests a more severe form of intestinal indigestion than does that of odorless gas

#### *Rôle of Abnormal Intestinal Flora*

—It is possible to have flatulence in the presence of a normal or even a specially restricted diet provided the intestinal flora is sufficiently abnormal. Such conditions obtain when large amounts of yeast cells are introduced as in the present vogue of yeast therapy. A more grave situation of this sort is encountered clinically in the case of persistent intestinal infections with presumably pathogenic bacteria. It is only necessary to recall the varied types of carbohydrate fermentation exhibited by the numerous intestinal bacilli of the colon and dysentery groups to appreciate the part played by these or similar organisms when they form the basis of a chronic intestinal infection. The classic studies of Hertter<sup>16</sup> will be recalled in this connection. He believed that in the "chronic saccharobutyric type" of intestinal putrefaction of adults, the activity of *B. aerogenes capsulatus* and of *B. putrificus* resulted in the production of the large amounts of  $H_2$  and of  $CO_2$  characteristic of this condition, whereas in

the "indolic type" of chronic excessive intestinal putrefaction in children, the large amounts of indol produced were probably due to the invasion of the small intestine by certain strains of colon bacilli

*Rôle of Gas Secretion from the Blood*—We have seen that gas passage through the intestine is a reversible reaction and that under certain circumstances gas may flow from the blood into the intestinal lumen. It is believed that normally this type of reaction is probably inconsiderable. The question naturally arises, "Is gas secretion from the blood ever of clinical importance?"

In this connection the work of McIver<sup>25</sup> again assumes particular interest. He observed that when either oxygen or hydrogen was injected into isolated loops of small intestine there was a progressive replacement of the absorbed gas by the blood gases, but that in each case, the greatest amount of new gas found was not oxygen or carbon dioxide, which exist in such large proportions in the blood, but nitrogen. This phenomenon is due not only to the fact that nitrogen occurs in the blood under a partial pressure of about  $4/5$  of an atmosphere (i.e. under a very high tension as compared with that of oxygen which is about one-fifth of an atmosphere), but also because this entire amount is held only in the form of a loose solution in the blood plasma whereas both the oxygen and the carbon dioxide exist almost wholly in chemical combination with the hemoglobin of the red cells. In other words the nitrogen is free to come out of the blood when the condi-

cent With these low figures must be contrasted the high incidence of flatulence in redundant colon (46%) We believe that this increase can be best explained by the mild and transient relative obstructions (spasms) which so often occur in the long loops of redundant intestines (see fig 3)

### C Flatulence Due to Deficient Gas Absorption

This important cause of flatulence may be considered under the following heads

1 *Interference with Mucosal Blood Supply*—An insufficient blood supply to the mucosa may result from a complete or partial volvulus, from portal obstruction, from mesenteric occlusion (thrombus, embolism, arteriosclerosis), and from general circulatory failure

Experimentally, Kato<sup>21</sup>, and more recently McIver<sup>25</sup> showed that if a loop of small intestine is filled with CO<sub>2</sub> about 90% is rapidly absorbed provided the portal vein is free If however, the portal vein is ligated only 40% of the gas is taken up in the same unit of time On the other hand it has been pointed out that such interference with the blood supply as is produced in the above experiment is extremely unlikely to occur clinically Indeed, Schoen<sup>31</sup> believes that the flatulence attributed to defective circulation might be better explained on other grounds He admits, however, that interference with the blood supply of the colon is much more serious than with that of the small intestine because vascularization is far less liberal in the former than it is in the latter organ

Despite these objections we believe that there is considerable clinical support for the impression that flatulence may be caused by defective circulation In the first place we are all too prone perhaps to underestimate the circulatory demands of the act of digestion Ordinarily, at least, we are not accustomed to regard the digestion of a meal as a load on the cardiovascular system in the same sense, for example, as we regard the ascent of a flight of stairs Yet it is the circulating blood that supplies the energy for the motor activities of peristalsis, the physical basis for the secretion of digestive juices, the thermoregulating mechanism for bringing foodstuffs of all degrees of cold or heat quickly and insensibly up or down to body temperature, and finally it is the circulation that furnishes the very vehicle for the removal, by absorption, of the products of digestion It should not be so strange therefore that one of the first signs of a failing circulation may be the inability to remove intestinal gases Alvarez quotes Stewart to the effect that differences in the tension of blood gases developing shortly after the onset of auricular fibrillation can upset the gas balance in the bowel wall even before venous stagnation has developed

The association of flatulence with hypertension is a striking finding In our series of cases this symptom occurred in almost one-half (46.5%) of the subjects with high blood pressure The exact significance of this phenomenon is not clear Flatulence is generally regarded as a common occurrence in arteriosclerosis, particularly in mesenteric arteriosclerosis In



FIGURE 1. Larva of *Trichoptera* (referred to as "larva") Appearance 24 hours after hatching

one case of proven coronary artery disease with probable mesenteric arteriosclerosis the gas passed by rectum was so rich in  $H_2S$  that it turned silver money in the patient's pockets black from the deposit of silver sulfid. In the syndrome described by Ortner<sup>28</sup> as *dyspiagia intestinalis intermittens angiosclerotica*, a peculiar "quiet" distention (so-called 'dead meteorism') of the ascending and transverse colon is associated with the characteristic painful seizures. The anatomical basis for the condition is assumed to be an arteriosclerosis of the superior mesenteric artery, leading to possible angospastic closure of the vessel or its branches.

It has frequently been pointed out, but may here bear repeating, that flatulence is a cause as well as a result of cardiovascular embarrassment. Thus not only does the elevation of the diaphragm produce mechanical pressure on the heart, but, according to Friedrich Kaufmann<sup>22</sup>, any increase in the intradominal pressure may cause a rise in the arterial tension through mechanical factors influencing the distribution of the blood. Hence it is easy to see how a vicious circle may be established.

*Interference with Mucosal Integrity*—It would appear reasonable to believe that when the intestinal mucosa is damaged by inflammation or ulceration, or its surface diminished by overproduction of mucus there would be increased difficulty with gas absorption and flatulence would result (see fig. 4). Our own experience strongly confirms this view, since colitis was found to be the most com-

mon important clinical condition (the chronic stomach bubble being excluded because of its rarity) in which flatulence was encountered (see table II). Indeed, it is possibly the presence of intestinal gas that gives rise to the well-known "belly-consciousness" complained of by these patients.

Contrary to the above clinical experience, Schoen opposes the view that mucosal inflammation causes flatulence and bases his opinion on experimental evidence. He poured corrosive fluids into the small intestine and found no interference with gas absorption. However, it is conceivable that repetition of his experiments, utilizing the large intestine instead of the small, might give results less at variance with clinical experience.

It may be of interest to recall that about 20 years ago the late Dr Seymour Basch of New York reported two analyses of gas specimens derived directly from the rectum of a case of chronic colitis ("chronic recurrent dysentery"). His findings, obtained on separate days, showed respectively

a  $CO_2$ , 4.1 per cent, O, 8.4 per cent,  $CH_4$ , absent, H, 8.4 per cent, 79.1 per cent, and  $H_2S$ , absent

b  $CO_2$ , 3.5 per cent, O, 18.4 per cent,  $CH_4$ , 5.1 per cent, H, 0.4 per cent, N, 72.6 per cent, and  $H_2S$ , absent

Basch felt that the oxygen figures in the second analysis may have been too high owing to possible air admixture in the rectal tube that was used. Somewhat similar figures are recently reported by McIver<sup>29</sup> in a case of diarrhea.

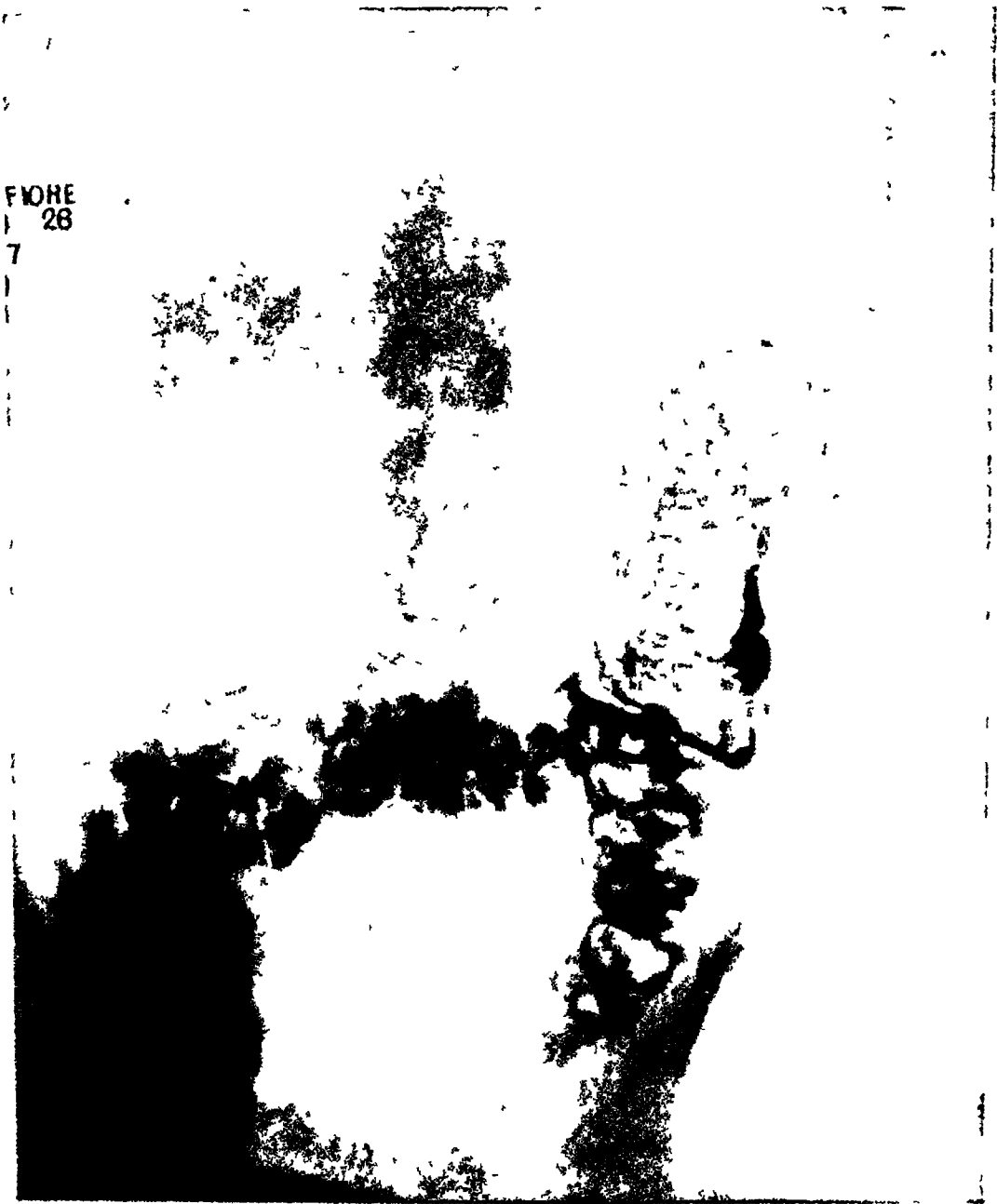


FIG. 28. Gross specimen of a case of probable tuberculous colitis. Appearance of the specimen after fixation.

*Interference with Muscular Tone (Intestinal Atony)*—The present trend of opinion seems to emphasize intestinal atony as a prime factor in the production of flatulence.

The form of this theory that most appeals to us is the following:

When for any reason the intestinal muscular tone is impaired, the lumen of the gut enlarges. This immediately lowers the intraintestinal pressure so that not only is gas absorption diminished but the possibility of gas excretion from the blood is enhanced. Soon a vicious circle develops since the greater the accumulation of gas the greater the depression of muscular tone due to stretching. This is particularly true if some of the gas locally produced is neuro- or myotoxic in nature. In this connection, Schoen mentions the tremendous depressing effect of certain amines derived from intestinal digestion, while McIver<sup>25</sup> reports a marked but transient drop in blood pressure from the intestinal injection of the highly absorbable  $H_2S$ .

The mechanism of intestinal atony in general is nowadays best explained on a neurogenic basis. It is believed that a characteristic depression of muscular tone results from some form of abnormal irritation of the inhibitory splanchnic nerve fibers. For example, adynamic or paralytic—i.e. non-obstructive—ileus is assumed to be due to such splanchnic irritation, because it has recently been shown that the ileus may be overcome by simply breaking the sympathetic reflex arc. This can be accomplished by anesthetizing either the (sensory) spinal nerve roots (Wagner)<sup>38</sup> or the (motor) splanchnic pathways (Ochsner)<sup>27</sup>.

Similarly, intestinal atony may result from even more remote nervous disorders. Thus, in disease or injury of the spinal cord involving the suprasegmental visceral nerve pathways, the lower (segmental) fibers are released from superior control. When this occurs the normal balance between the inhibitory (sympathetic) and excitatory (autonomic) innervations is assumed to be upset in the sense that it is the sympathetic influence that predominates (Feltkamp)<sup>18</sup>. Accordingly, whenever the intestinal distribution is involved, ileus with meteorism develops. Whether this theory be accepted or not, meteorism is known to be a striking complication of such upper cord conditions as trauma, syringomyelia, combined sclerosis, and pernicious anemia. Elsberg<sup>10</sup> has pointed out the occurrence of ileus following laminectomy in the lower dorsal region.

That the nerve pathways are fundamentally concerned in the development of meteorism in such toxic states as peritonitis, typhoid fever, pneumonia,<sup>4</sup> and general sepsis, is more than probable. Similarly, a neurogenic mechanism may be safely assumed to underlie the hysterical form of pneumatosis such as that described many years ago by Valentiner<sup>37</sup>. Whether or not the lesser forms of distention more commonly encountered in practice are of neurogenic origin is not yet definitely established, although the fact that flatulence occurs most often when patients are fatigued or emotionally unbalanced seems to lend obvious support to such an hypothesis.

\*For gas analysis of intestinal flatus in distended pneumonia patients see McIver<sup>26</sup>.



### III THERAPY OF GAS IN THE INTESTINE

*Nervous Factors*—Flatulence, as well as bowel troubles in general, is known to be commonly associated with nervous and mental symptoms. Indeed, owing to the nature of the disability, patients are often prone to be unduly depressed and morbid over their condition and to exaggerate what they regard as their repulsiveness to society. On the other hand this symptom may be but an expression of a more general neurosis. Its onset may at times be abrupt, following a psychic shock or trauma.

Since flatulence is, in this sense, a functional condition, treatment must be planned on a sufficiently comprehensive basis. This implies attention to such major hygienic measures as regular habits of living, rest and recreation. Psychic and emotional rest is particularly important, but this is not always easy to bring about, despite much patient and reassuring encouragement on the part of the physician. Perhaps the most satisfactory medication for the general treatment of flatulence is a mild sedative—we use a bromid and chloral mixture—which may have to be continued for long periods. Carminatives also we believe, have their place in the mild cases.

In those individuals who exhibit a spasmophilic or vagotonic makeup, belladonna or its alkaloid, pushed if need be to the point of cycloplegia, is very helpful. In Balint's "tympanismus vagotonicus" <sup>2</sup> the abdominal distention is said to be removed by atropin and reproduced by physostigmin. However, as will be seen directly, physostigmin itself is sometimes of decided benefit in this condition. Thus, in neurologic ileus, where the distention is due to injury or disease of the spinal cord, injections of physostigmin or of pituitrin (see below) possibly constitute the best treatment now available. The use of these drugs in toxic distentions (pneumonia, typhoid, sepsis, late intestinal obstructions) though less likely to be followed by relief, is also to be recommended. Pilocarpin is sometimes useful, it acts in the same way as physostigmin, by stimulating the autonomic fibers. The antidote to both these drugs is atropine.

*Air Swallowing*—Most air is introduced into the stomach by neurotic belching. Patients afflicted in this way should be taught the difference between voluntary belching, which always introduces some air into the stomach, and spontaneous belching, which expels air only, and they should be directed to control the former habit. In paroxysmal belching, or in air sucking (cribling), having the patient bite on a large cork may break up the attack. General sedatives are of course indicated.

In our patients with chronic stomach bubble it was found that gastric hyperacidity occurred fairly often. In some of the cases, alkalies seemed to

break up the spasm, in others belladonna, but many proved refractory to treatment. In such obstinate cases, forcible dilatation of the cardia might be considered, though it may with justice be objected that the cure is worse than the disease.

*Diet*—Not much need be added to what has already been stated or implied in the text that has preceded. Avoidance of an excess of cellulose and the careful selection and cooking of vegetables should take care of all ordinary requirements. In some individuals raw whole milk should be entirely eliminated from the diet. For the majority of cases, a full well-balanced regime, such as an expanded Schmidt diet, suffices. Fluids at meals, especially those that can be drunk quickly, should be avoided, in order to minimize air swallowing.

In patients requiring more active treatment, a preliminary dose or two of castor oil is desirable to clear out old residues. Possibly a day of starvation may be interposed before feeding is resumed. The amount and type of food depends on the degree and nature of the flatulence. In patients with particularly foul flatus, a course of acidophilus milk in increasing doses seems now to be the best initial procedure. The diet may then be built up gradually as in the usual management of putrefactive intestinal dyspepsia. Similarly, cases of fermentative dyspepsia will respond in their turn to appropriate dietetic procedures.

*Post-Operative Distention*—As regards the prophylaxis of post-operative distention, we quite agree with

Alvarez that it is time to discard the ancient practice of purging patients routinely as a preparation for surgical intervention. In addition, too long a period of pre-operative starvation is unnecessary.

The simplest treatment for post-operative distention resulting from air swallowing, is postural, the object being to encourage spontaneous belching. This may be accomplished, in favorable cases, (1) by putting the patient into as nearly an upright position as his wound will permit, and (2) by turning him on his left side and thus bringing the cardia uppermost. If these measures fail, a tube should be passed into the stomach for the purpose of puncturing the stomach bubble. Intubation with a large tube (size 36 to 40 F) of the proper consistency is a speedy and perfectly safe procedure in the hands of an experienced operator. This form of treatment has the additional advantages of removing obnoxious fluids from the stomach and of permitting rapid and thorough lavaging. The intubation may of course be repeated at appropriate intervals.

When the gas accumulation is principally intestinal, the mere introduction of a rectal tube suffices to relieve many patients whose difficulty is due to ineffectual abdominal wall contraction. In most cases soothing oil injections are preferable to irritating enemas. When the meteorism appears to be due to intestinal atony, the best results, according to some, are obtained from drugs which increase smooth muscle tonus. Pituitrin, 0.5 to 1.0 cc by deep intramuscular or hypodermic injection is perhaps the most com-

monly used medication. It is often advisable to follow the injection in about half an hour by a large enema (2 quarts) to increase the intestinal contents and thus aid the expulsion of gas. The use of physostigmin salicylate in doses of  $1/40$  to  $1/20$  grain has given good results in actual practice. The careful observations of Martin and Weiss<sup>21</sup> showed that the larger doses (up to  $1/16$  grain), administered intramuscularly, proved successful in relieving otherwise rebellious cases of non-toxic abdominal distention. Gas was belched or expelled from the rectum within 10 to 40 minutes after an effective dose was given. They saw no cardiac depression in even desperately sick patients. Pilocarpin hydrochlorid, in doses of  $1/12$  grain hypodermically is also said to be of value. Schoen has shown experimentally that  $\text{CO}_2$  absorption is promoted by the increase in intestinal tone that accompanies pilocarpine administration.

In contrast to the above recommendations, McVey<sup>22</sup> warns against drugs which increase peristalsis in post-operative distention and favors the use of morphine to quiet intestinal movement. Finally, the successful results following both spinal and paravertebral anesthesia in paralytic ileus should be borne in mind. They have already been mentioned in the section on the mechanism of intestinal atony in his relief of similar conditions.

lating diet. Fortunately this condition usually subsides spontaneously after the new regime is established, or at the most, after administration of a mild sedative mixture, or an occasional saline enema.

In constipation due to redundancy of the colon, flatulence is much more likely to be a troublesome feature. Once the situation is correctly appraised, the gas distress usually responds to appropriate treatment.<sup>19</sup>

*Colitis*—In cases of simple colitis, that is, colonic irritability not associated with infection or ulceration, the flatulence yields to simple measures. In our experience appropriate simplification and regulation of the diet, mild sedatives, and sometimes belladonna, constitute an effective therapeutic program. In addition, as described elsewhere<sup>20</sup>, we prescribe half-ounce or ounce doses of a mixture of equal parts of barium sulphate and kaolin once or twice daily in fermentac, cocoa or thick cereal, according to the preference of the patient. These inert powders seem to depress mucosal irritability and thus aid gas absorption. It is possible that large doses of loose charcoal would act in similar fashion although we have not tried this, and have obtained an impression of uniform failure from the use of the more or less compressed charcoal tablets commonly employed by patients.

In flatulence associated with gastrointestinal enterocolitis, whether due to achylia gastrica or following extensive gastric resections, the administration of hydrochloric acid in appropriate dosage is often helpful.

In cases of colitis gravis, such as those characterized by infection (fever) and ulceration (hemorrhage), the same treatment appears indicated as has been outlined for simple colitis. However, we have never been able to satisfy ourselves that the welcome remissions that occasionally punctuate the course of this distressing disorder could be ascribed to any of the therapeutic measures we have employed.

*Cardiovascular Insufficiency* — In cases of general heart failure the best treatment for the flatulence is obviously the control of the cardiac condition. This means, ordinarily, rest and digitalis. Under the head of rest however, the important idea of digestive rest should not be neglected. This is carried out by a proper restriction and simplification of the diet. In very sick or edematous patients who take milk well, the Karrel diet is often sufficient to control the flatulence adequately. In other cases the ordinary convalescent ulcer diet or the Schmidt intestinal diet proves satisfactory. All these regimens are based on the principle of frequent small feedings of readily digestible foodstuffs, and thus automatically avoid the sudden excessive demands on the digestive circulation produced by the usual large repasts.

The flatulence associated with high blood pressure, as well as with arteriosclerosis with or without hypertension, is also treated by rest of the digestive tract. Here one must observe the principle of split feedings with foods least likely to produce gas, and the patient should be further cautioned to rest and relax an appreciable time before, and particularly after, eating.

Failure to take these precautions may result in anginal attacks or, in cases of advanced coronary arterial disease, in a fatal seizure.

In patients with cardiovascular disabilities the control of constipation is important. However, inasmuch as the usual rough diet is absolutely contraindicated, recourse must be had to the freer use of cathartics. If mineral oil works well, the problem is solved. Otherwise an effective and popular procedure is the administration of a saline cathartic. This is best given in concentrated form on a fasting stomach and should be followed immediately by a glassful of water. Breakfast should be delayed for at least half an hour. Both the flatulence and the increased blood pressure often respond well to this treatment. Cures at the popular spas are sometimes followed by relief for considerable periods.

For the acute distentions and recurrent painful seizures of dyspepsia arteriosclerotica, diuretin (theobromin sodium salicylate) is recommended by Ortner and by v Noorden<sup>30</sup>. The dose is 0.5 gram three times daily for months at a stretch. We have had no experience with this medication.

*Carminative Treatment* — Carminatives have long held a place in the treatment of flatulence. Just how they act is not clear, though they seem effective in many mild cases. Their influence, presumably reflex, is said to be slightly cathartic, yet at the same time mildly anesthetic and antispasmodic.

Perhaps the most useful types of carminatives, as shown by long experience are

Group 1 Ether, chloroform, the volatile oils, and the concentrated alcoholics. Examples are spiritus aetheris (one teaspoonful), Hoffman's anodyne (one teaspoonful), spiritus menthae piperitae (5 to 20 drops), crème de menthe, cointreau, Benedictine, etc. A favorite hospital prescription, according to Bastedo<sup>5</sup> is

R/ Compound spirit of ether  
Aromatic spirit of ammonia  
Compound tincture of lavender  
Spirit of chloroform  
aa 15 minims

Group 2 Herbs or teas, as in the following continental prescriptions (Strassburger)<sup>11</sup>

R/ Semen foeniculi  
Fruct anisi  
Fruct cavi  
Folia menthae pip aa 25 0  
M ft pulv Sig Brew into a tea,  
one tablespoon to each cup of  
water  
R/ Cinnamon  
Ginger aa 35 0  
Nutmeg  
Cardamom aa 15 0  
M ft pulv Sig 10 to 20 as  
needed

Group 3 Carminative enemas. The following combinations are used (Bastedo). Oil of turpentine, one-half ounce, or tincture of asafoetida or spirit of peppermint, 1 dram, added to 8 spoonfuls castor oil or to 8 ounces or 100 cc of solution of chamomile

for which we could find no adequate reason. In some instances these attacks occurred in obviously sensitive persons and could then be attributed to an excitability of the involuntary nervous system that we were unable to quiet. In other cases the patient seemed placid enough, yet the attacks persisted despite all we could do to control them. The abdominal films of one such case showed several large dense shadows of calcified mesenteric glands. It is conceivable that these masses acted as foci of irritation to nerve pathways and thus brought on the attacks of gas. Further observations along these lines are obviously desirable.

#### IV SUMMARY

1 Intestinal flatulence ranks third among the ten most common complaints of private patients suffering from digestive disorders.

2 In general, flatulence may be caused by excessive gas intake or production, by deficient gas expulsion, or by deficient gas absorption.

3 Atmospheric air plays a definite but not necessarily a major role in the etiology of flatulence.

4 The chronic stomach bubble is a rare but striking cause of flatulence.

5 The diet may cause flatulence, but this factor can be readily controlled in most cases.

6 An abnormal intestinal flora plays the leading rôle in the flatulence of intestinal infections.

7 Gas may be secreted from the blood under certain circumstances. At times, this may be an important cause of flatulence. Therapy is presented

for the belief that the greater part of the gas so secreted is nitrogen

8 Flatulence from deficient gas expulsion arises in complete obstruction and in redundant colon. Constipation is not a frequent cause of flatulence

9 Deficient gas absorption is an important cause of flatulence. It may result from interference with mucosal blood supply, destruction of mucosal integrity, or depression of muscular tone

10 Interference with mucosal blood supply occurs in volvulus, portal obstruction, mesenteric vascular occlusion or sclerosis, and general circulatory failure. The incidence of flatulence in hypertension was strikingly high (46%) in our cases

11 Interference with mucosal integrity is best illustrated in colitis. Almost one-half of our colitis cases showed flatulence

12 Interference with muscular tone (atony of the intestine) is probably a very important cause of flatulence. Atony may result from various neurogenic or myotoxic causes and thus retard gas absorption and favor gas excretion from the blood

13 In our opinion, a theory of flatulence which would assume a sudden development of intestinal atony with rapid filling of the bowel by blood gases, chiefly nitrogen, would best account for many of the sudden baffling distentions encountered clinically

14 Such a theory would explain the flatulence of neurologic ileus, of toxemias associated with severe pneumonia, sepsis, and typhoid fever, of various hysterical states, as well as that encountered post-operatively

15 The treatment of the more important clinical types of flatulence is discussed

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# Lung Volume and Its Variations\*†

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THE statement that respiratory exchange in the lower branches of the bronchial tree, the bronchioles and the alveoli is carried on chiefly by diffusion, is probably correct up to a certain point. However, the importance of respiratory movements in the ventilation of the air sacs cannot be relegated to a rôle of minor importance. Without such movements the respiratory function fails to support life even under artificial conditions of enormously increased diffusion pressures. The efficiency of the ventilating system inaugurated by the respiratory movements is obviously most important in abnormal pulmonary conditions.

On approaching the subject of pulmonary ventilation it is necessary to describe briefly certain terms in common use in order that no confusion of definition may arise. For our present purpose six such definitions are necessary,—

- a Vital Capacity—The volume of air expired by a maximum expiration after a maximum inspiration,

- b Residual Air—The volume of air remaining in the lungs after a maximum expiration,
- c Total Lung Volume—The sum of (a) and (b) or the total capacity of the lungs at the end of a maximum inspiration,
- d Middle Capacity—This term is applied to that quantity of air which is in the lungs if the breathing be stopped midway between an average resting inspiration and expiration
- e Functional Residual Air—By this term is implied the amount of air which is in the lungs at the end of an average resting expiration. It would consist of the residual air as described in (b) plus the volume of air represented by the volume expelled from the lungs between an average resting expiration and a maximum expiration, or what is known as the (f) reserve air

Of these measurements the vital capacity and the reserve air can be readily determined and this by an ordinary spirometer. The measurement of the total lung volume, residual air, and functional residual air can only be determined by a more complicated method such as that described by Van

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Slyke and Binger<sup>1</sup> We have used such a method. The principle of this method depends upon the breathing of a rich oxygen mixture containing an accurately known quantity of hydrogen approximating the volume of nitrogen in the lungs at the time of the beginning of the determination. After some minutes of breathing through a closed circuit there is a thorough mixing of the hydrogen and nitrogen in the lungs as well as the rest of the circuit. The percentage concentrations of  $H_2$  and  $N_2$  are then determined. Since

$$\frac{\text{initial vol of } N_2 \text{ in lung air}}{\text{initial vol of } H_2 \text{ in mixture}} = \frac{\text{final \% } N_2 \text{ in mixture}}{\text{final \% } H_2 \text{ in mixture}}$$

$$\text{vol } N_2 = \text{vol } H_2 \times \frac{\text{per cent } N_2}{\text{per cent } H_2}$$

But nitrogen constitutes 79.1 per cent of air, therefore, the volume of air in the lungs at the commencement of the determination is

$$\frac{\text{vol } N_2 \times 100}{79.1}$$

minus dead space in the apparatus. It is necessary, however, to know the exact phase of respiration at which the respiration of the hydrogen-oxygen mixture begins. This is obtained from a tracing taken with a spirometer. In such a tracing may be incorporated the normal respiratory cycle where the estimation is made (fig. 1)

To calculate the total lung volume, that portion of the vital capacity lying above the point at which the estima-

tion was made, is added to the lung volume as measured by the nitrogen-hydrogen ratio. Similarly the residual air is calculated by subtracting that portion of the vital capacity lying below the point at which the estimation was made.

The functional residual air varies, depending upon the relative position of the middle capacity or, in other words, the position in the total capacity of the lungs where average respiration at the moment is taking place. This we know to be changeable not only in different people but in the same person under varying conditions. At the moment sufficient data is not available to discuss these changes in middle capacity but it would seem to change in normals under different conditions of rest and work, of position, of reflex stimuli, and probably many other unknown factors. Until this subject has been more thoroughly investigated it is difficult to arrive at any conclusion as to its influence on pulmonary ventilation.

The efficiency of pulmonary ventilation would appear to rest upon the relationship between the residual air and the total lung capacity. In normal individuals this has been found, by different workers, to vary between 26% and 33%, the variation depending upon the methods used. In our experience with a number of healthy adult males it has been found to average 33%.

On considering the different thoracic lesions which might interfere with pulmonary ventilation, it is possible to divide them into two main classes, first, those conditions which although encroaching upon the total

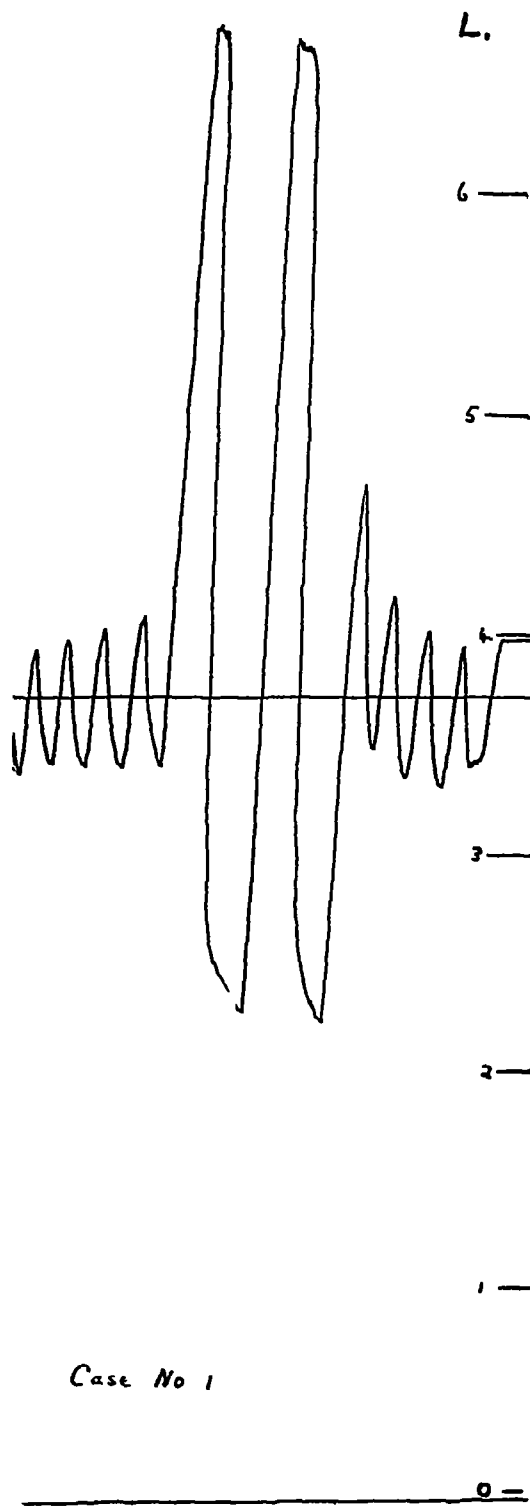
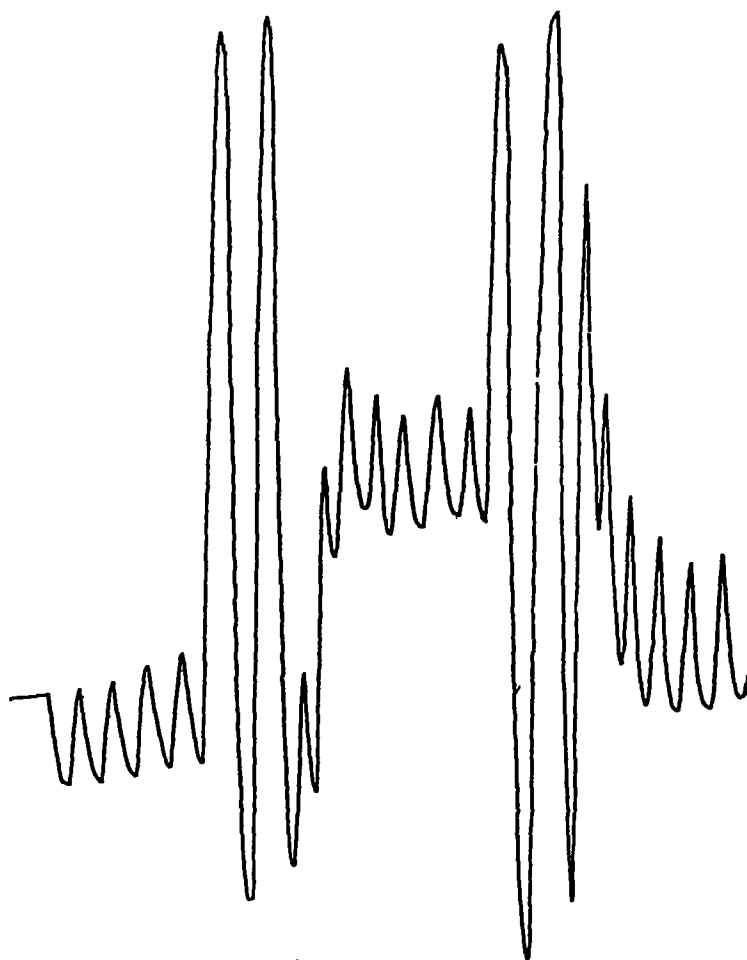


FIG 1 Normal Case Tracing of respiratory movements with vital capacity (a) Point at which estimation of lung volume was started Numerals represent litres of total lung capacity From end of forced expiration to base line represents residual air



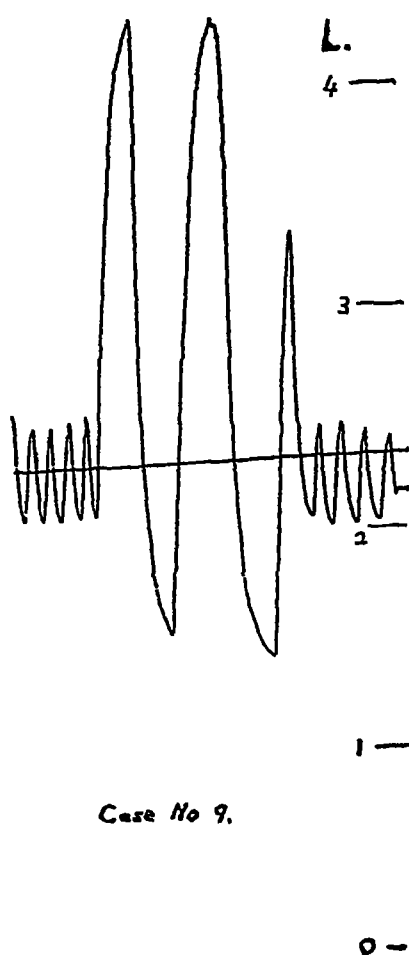
#### Case No 4

FIG 2 Tracing showing variations in so-called mid-capacity

alveolar area of the lung at the same time do not interfere with the expansile power of the uninvolved portions. Examples of such are hydrothorax, pneumothorax, and localized tuberculosis. The second class includes those conditions of the lungs or thorax which interfere either with the expansibility of the lung or the efficiency of the respiratory muscles. Examples of such are found in chronic passive congestion of the lungs due to circulatory failure, chronic emphysema, paroxysmal asthma, and paralysis of the intercostal muscles or diaphragm or severe pleuritic pain. There are a number of conditions which cannot be clas-

sified at the moment in either of these categories, such as acute lobar pneumonia, miliary tuberculosis, diffuse bronchiolitis and massive pulmonary collapse.

It has usually been considered that a reduction in vital capacity is an index of the efficiency of pulmonary ventilation. We have found that this is not necessarily the case. It is a common observation that under certain circumstances vital capacity may be considerably reduced but still the individual need not suffer from dyspnea or any respiratory distress. We believe that it depends upon the ratio between the total lung capacity and



Case No 9.

FIG 3 Case of pleurisy with effusion, left-sided Legend as in Fig 1

the residual air as to whether dyspnea under ordinary conditions will ensue

We have found in cases of pleurisy with effusion and in artificial pneumothorax where the opposite lung is in good physical condition, that although the vital capacity may be reduced to a pronounced degree, the ratio between the total lung capacity and the residual air remains within normal limits. In such cases there is no dyspnea or respiratory distress within ordinary limits of exertion. Similar observations have been made by Garvin, Lunds-

gaard and Van Slyke<sup>2</sup> in cases of pulmonary tuberculosis

In regard to the second category our investigations in cases of circulatory failure have shown a more or less direct relationship between the severity of the pulmonary symptoms and the reduction in vital capacity. This merely confirms the findings of many previous observers. These pulmonary symptoms have been considered in great part to be intimately associated with this reduction. But this explanation could not be reconciled with a similar reduction in vital capacity

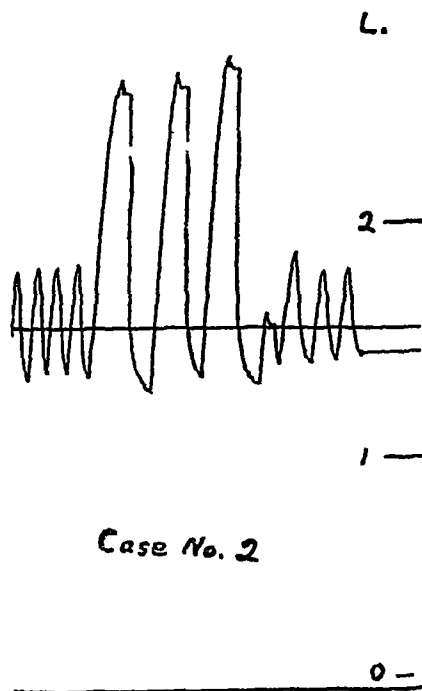


FIG 4 Case of circulatory failure Legend as in Fig 1

found in category I which was not accompanied by respiratory distress. We have found, however, a striking difference in the amount of residual air in these two types of cases. In cases of circulatory failure with a reduced vital capacity, instead of the residual air diminishing proportionately and thus maintaining the same ratio to the total lung volume, the residual air may not only relatively but also absolutely increase. This increase is brought about by a progressive encroachment of the residual air upon the reserve air, so that the unventilated area of the lung at the end of a forced expiration becomes greater and greater. It is not unusual to find in cases of circulatory failure that the reserve air has completely disappeared and that a forced expiration is not any greater than an average resting expiration. We have found that the residual air may amount

to more than 50% of the total lung capacity. This corroborates the findings of Binger<sup>3</sup>. It is quite obvious under these circumstances how difficult it would be for an individual so placed to carry on proper alveolar ventilation. We have found that as the respiratory symptoms diminish there is a progressive reduction in the ratio of the residual air to the lung capacity, while as the symptoms increase the converse occurs.

A similar condition of affairs has been found by Lundsgaard and Schierbeck<sup>4</sup> to exist in cases of pulmonary emphysema.

In considering the underlying cause of such a symptom as dyspnea in any individual case we are frequently confronted by a number of intimately connected factors all of which may contribute towards the eventual result. Therefore, we do not wish to over-

emphasize the importance of these factors in its relation to the other factors, but it seems that sufficient attention has not been given to the variations in the conditions existing in pulmonary ventilation. Furthermore, in view of the advances that have been made in the understanding of the chemical and nervous regulation of the actual conditions of pulmonary function, the work carried out in this field has been mostly lost sight of. We merely give the importance of the actual physiology of pulmonary ventilation while at the same time keeping it in its proper perspective in relation to the other factors which regulate respiration and pulmonary ventilation.

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# A Study of the Effect of Chronic Pulmonary Diseases on the Volume and Composition of the Blood\*

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WITH the phylogenetic development of a hemolymph system, the contact of respiration and circulation became complete. Throughout all the metamorphosis that bridges the gap between primitive organs and the complicated bodily systems of vertebrates, this relationship is maintained, and the mutual dependence of one on the other is strengthened almost in direct ratio to the multiplication of the necessities of complicated processes of life.

These ancient functions of respiration and circulation of blood are so vital and so fundamental a part of life that they are protected by a physiologic reserve far in excess of any requirement that could be anticipated by any of the exigencies of natural life. The body, however, is beset by many agencies that wear down and dissipate physiologic reserve, sometimes of one, sometimes of the other of these two functions. Reserve in the function bearing the brunt of assault prevents disaster. Compensatory factors in the function indirectly affected are ulti-

mately inevitable and serve to stabilize the actions of both. Regardless of handicap, if competency is to be maintained nutrition must be supplied to near and distant parts, oxygen must come to the blood and through it to the tissues.

It has long been recognized that certain changes of a compensatory nature may occur in the blood in disturbance of the cardiorespiratory system especially when normal pulmonary ventilation is impaired. Chronic emphysema, chronic asthma, pulmonary fibrosis, and obstructive conditions furnish the usual clinical examples of conditions which impair the respiratory and circulatory functions. Lowered oxygen tension in the arterial blood, or arterial anoxemia, may induce erythrocytosis as measured by the concentration of erythrocytes in the peripheral blood. This response of the blood is probably common to that occurring in other conditions which produce anoxemia, such as the erythrocytosis which occurs after long residence at high altitudes. Likewise, experiments in the oxygen chamber, under conditions of lowered oxygen tension, have revealed hyperactivity of the bone

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marrow Recent investigations by Dallwig, Kolls, and Loevenhait, on animals confined at normal barometric pressures but at low oxygen tensions, have emphasized the proportion existing between the degree of anoxemia and the resulting erythrocytosis The erythrogenesis resulting from residence at high altitudes may not be due entirely to lowered oxygen tension Other factors have been suggested, such as the effects of lowered atmospheric pressure, of cold, of light, of dryness of the air, of increased loss of water, of rapid evaporation from the surface of the body, of redistribution of the peripheral blood, and of the vasomotor changes Regardless of these contributing effects, there seems to be no reason to doubt that anoxemia is the exciting factor in stimulating the changes in the blood

The blood, in clinical conditions accompanied by chronic disturbance of pulmonary oxygenation, has been studied in relation to the concentrations of hemoglobin and erythrocytes in the peripheral blood Data concerning the circulating volume of blood, plasma, and hemoglobin, and correlative information on the oxygen of the blood are lacking The work of Smith and his associates, on the effects of short periods of residence at high altitudes, has been studied by means of the dye method for determining volume of blood and of plasma This condition, however, does not simulate that occurring in diseases in which chronic conditions of anoxemia exist over a period of years The time seemed apropos for a fuller investigation of the possible changes occurring in the circulation and in the

blood in diseases in which chronic anoxemia may be suspected to be present The problem is of more than academic interest, because frequently the question is raised whether a diagnosis of primary or of secondary polycythemia should be made when, in a given case, erythrocytosis and cyanosis are present

#### MATERIAL STUDIED

The following groups of patients were studied

(1) Twelve subjects with chronic bronchitis and emphysema, associated with significant grades of cyanosis, (2) two subjects with polycythemia vera and splenomegaly, complicated by chronic pulmonary disease, emphysema or asthma and exhibiting excessive grades of cyanosis, and (3) one subject with an excessive degree of cyanosis and who gave evidence of hypertrophy of the right ventricle of the heart with myocardial insufficiency, the clinical diagnosis was Ayerza's disease

The main study was of the patients in group 1, the patients in the other groups are merely referred to for comparison

#### METHODS OF STUDY

Concentration of the erythrocytes and hemoglobin was determined in the peripheral blood A combination of Haden's<sup>4</sup> and Osgood's methods of determining the acid hematin was employed for the estimation of hemoglobin The volume of blood and of plasma each was determined by the dye method<sup>7</sup> Congo-red was used and a mixing time of three to six minutes was allowed The volume of circulating hemoglobin was studied by obtaining the product of the total blood



volume and the grams of hemoglobin for each 100 c c of blood. The oxygen content and percentage saturation of the arterial and of the venous blood was determined by the Van Slyke volumetric method. Blood was obtained by arterial puncture of the brachial or of the radial artery. The percentage saturation of hemoglobin in the individual erythrocyte was calculated according to the method of Haden<sup>5</sup>. The vital capacities were determined and charted as the actual and calculated values.

#### VALUES FOR NORMAL PERSONS

*Hemoglobin*—The average normal concentration of hemoglobin in normal persons is 15.6 gm for each 100 c c of blood, this value in males is 16.4 and in females, 14.2. There is a definite difference in the mean values in males and females. In females the mean value for the volume of circulating hemoglobin is 12.2 gm for each kilogram of body weight, and 44.2 gm for each square meter of body area, in males the corresponding values are 14.7 gm for each kilogram of body weight and 54.1 gm for each square meter of body area.

Haden's values for the normal volume and hemoglobin content of the single erythrocyte are as follows. The normal value for the volume index is 1, for the saturation index is 1 and for the average erythrocyte in cubic centimeters is  $9.2 \times 10^{-11}$ . The grams of hemoglobin in the average erythrocyte is  $3.12 \times 10^{-11}$ , or an actual percentage of hemoglobin in the individual erythrocyte of 33.9, with a range of 32 to 36.

*Hematocrit values*—The normal hematocrit value, using dry sodium ox-

alate as an anticoagulant, is 42 per cent by cells. This has been shown by Whipple and his associates to be approximately 3 per cent less than the true normal volume obtained by using solution of sodium oxalate as an anticoagulant, the wet method.

*Blood volume*—The range of volume of blood has been well established in a series of normal subjects, of average weight and height, by Rowntree and Brown. The normal range is from 70 to 97 c c for each kilogram of body weight, with a mean value for normal persons, males and females taken together, of 87.7 c c. As is well known, the variations in body weight in normal subjects are fairly great. When calculated on the basis of body area, the mean value or blood volume for normal persons of both sexes taken together is 3278 c c for each square meter of body area. The variations due to slight grades of underweight and overweight is less marked according to body area than according to body weight. The mean plasma volume for normal subjects is 51.2 c c for each kilogram of weight, and 1920 c c for each square meter of body area. The variations in plasma volume that are coincident with conditions of underweight and of overweight in normal subjects are proportionately the same as the variations in blood volume under like conditions.

The question as to whether blood volume is determined by body weight or body area has been discussed by Dreyer and Ray, and by Rowntree and Brown. Correlation coefficients have indicated a higher correlation of blood and of plasma volumes to body

area than to body weight. For the present, we have expressed the blood and plasma volumes in relation both to body area and to body weight, our deductions have been based largely on the changes found according to weight, as much of the data previously published has dealt with this relationship.

Considerable difficulty is encountered in determining abnormalities in the blood volume in disease of subjects who either are abnormally underweight or overweight. In order to determine whether the changes in blood volume are actual or only apparent on the basis of body weight, we have attempted to obviate this difficulty by expressing the blood volume of the patient according to both his body weight and his body area, and then calculating his blood volume according to his ideal weight for his height and age by actuarial standards. The last value is designated as blood volume according to corrected body weight. Eventually, blood volume may be expressed as plus or minus from zero or normal. This question has been carefully discussed by Rowntree and Brown.

The figure for oxygen capacity of normal blood is 21 volumes per cent. The oxygen capacity of arterial blood under normal conditions is 20 volumes per cent and the percentage saturation, 95.6 per cent. The corresponding values for venous blood are 14.5 volumes per cent and 70 per cent.

The normal vital capacity varies with height, weight and body area. The actual and estimated volumes in the cases studied are given in table 1.

STUDY OF TWELVE CASES IN GROUP I

Of the twelve cases (table 1) selected for study, one was that of a

woman and the others were men. All but four patients were more than fifty years of age, neither obese nor undernourished patients were in the group. The actual weight of each patient compared favorably with the ideal weight for his height and age. The three most striking variations from ideal weight were in cases 2, 3 and 11. In case 3 the weight was 18 kg more than the ideal weight for height and age, and this discrepancy made a considerable difference in the estimations of the volume of the blood. The same was true in the other two cases, but to a much less degree.

*Hemoglobin*—The values for hemoglobin that were employed in this study were as follows (tables 2, 3 and 4) (1) the grams in each 100 c c of blood, (2) the grams of circulating hemoglobin for each kilogram of body weight and for each square meter of body area, and (3) the percentage in the individual erythrocyte. The grams of hemoglobin in each 100 c c of blood varied from 11.5 to 20 with a mean value of 16.5. In six cases the values were in excess of 16.4 gm which is the normal value for males. The total amount of circulating hemoglobin was 14.9 gm for each kilogram of body weight and 554 gm for each square meter of body surface. In order to determine the percentage of hemoglobin in the individual erythrocyte the volume index first was calculated. The average value for the volume index was 1.05. The saturation index was 1.22, the volume of the average cell was  $8.86 \text{ c c} \times 10^{-11}$ . The number of grams of hemoglobin in the average cell was  $3.64 \times 10^{-11}$ . The average value for the actual percentage of hemoglobin in the erythrocyte was 14.5 per cent.

TABLE I  
CLINICAL OBSERVATIONS IN TWELVE CASES IN WHICH THERE WAS CHRONIC BRONCHITIS, EMPHYSEMA, AND SIGNIFICANT GRADES OF CYANOSIS

Case	Complaint	Blood pressure mm mercury		Vital capacity, c	Thoracic roentgenogram	Electro-cardiogram	Clinical observations	Diagnosis	Comment
		Systolic	Diastolic						
1	Asthmatic attacks, dyspnea, orthopnea, cough, sputum	105	80	3128 to 4480	Negative	Rate 63, sinus rhythm, QRS notched in lead III, left ventricular preponderance	Typical emphysema, cyanosis, pleural rub	Emphysema, chronic bronchitis, nasal polyps, sinusitis	Hardened cartilages, nonelastic chest
2	Dyspnea	102	58	3625 to 4735	Negative	Sinus rhythm	Cyanosis, dyspnea, wheezing râles	Emphysema, asthmatic bronchitis, nasal polyps	Six weeks' duration only
3	Dyspnea, dizziness, thoracic pain	130	94		Negative	Sinus tachycardia, rate 100	Dyspnea, wheezing râles, heart enlarged	Emphysema, bronchitis, arteriosclerosis, obesity	Circulation competent
4	Dyspnea, dizziness, thoracic pain	108	70	3058 to 4522	Pneumokoniosis		Diffuse râles	Emphysema, pneumokoniosis, silicosis	Fibrosis of lung resulting in lowered vital capacity, 33.5 per cent of normal

5	Dyspnea, cough, dyspepsia	156	90	2911 to 4255		Rate 71, sinus rhythm, left ventricular preponderance	Heart and breath sounds distant, voluminous lungs	Emphysema, bronchitis, myocardial degeneration, coronary sclerosis	Years of respiratory and circulatory difficulty with gradual heart failure, no erythrocytosis
6	Dyspnea, cough	124	64		Bilateral pulmonary tuberculosis		Typical emphysema, barrel-shaped chest, dyspnea severe	Emphysema, chronic bronchitis, old tuberculosis	Very frail, very dyspneic, very low vital capacity
7	Dyspnea, hoarseness	130	70	4449 to 4000	Heart enlarged		Typical emphysema, dyspnea, marked cyanosis	Emphysema, chronic bronchitis, arteriosclerosis, coronary sclerosis	Heart enlarged but competent, question of polycythemia
8	Dyspnea, cough, profuse sputum, weakness	140	80	4648	Old lesion both upper lobes, pleural thickening		Dyspnea, cyanosis, râles in lungs, enlarged normal heart	Emphysema, mitral endocarditis	Compensated heart
9	Dyspnea, palpitation, asthma	152	80		Extensive fibrosis of both lungs		Râles throughout lungs, asthmatic breathing	Emphysema, asthma	Exophthalmic goiter, central aneurysm, or brain tumor
10	Dyspnea, cough, epigastric pain	120	90		Heart enlarged	Rate 75, sinus rhythm, right ventricular preponderance, P wave notched in leads II and III	Râles throughout lungs	Emphysema, asthmatic bronchitis, septic tonsils, inguinal hernia	Asthma ceased three years previously

11	Dyspnea, cough, sputum	110	80	1993 to 4572	Negative	Rate 81, sinus rhythm, right ventricular preponderance, QRS wave notched in leads II and III	Long narrow chest râles, no cyanosis	Emphysema, bron- chitis, congenital pulmonary defect (?)	Dyspnea severe and produced invalidism, vital capacity re- duced 57 per cent
12	Dyspnea, cough, sputum	108	80		Healed tuberculo- sis in upper lobe of right lung	Rate 109, sinus tachycardia, right ventricu- lar preponder- ance, exagger- ated P wave in lead III	Sibilant râles throughout, asthmat- ic breathing, heart sounds distant	Asthmatic bronchi- tis, nasal polyps, chronic nephritis	Polycythemia considered

TABLE 2  
VOLUME OF BLOOD AND PLASMA IN CASES OF EMPHYSEMA AND ASTHMA

Case	Age	Sex	Weight, kg	Ideal weight for height and age, kg	Hemoglobin, gm in each 100 cc of blood	Cells by the hematocrit, per cent	Erythrocytes, millions	Blood volume			Cc for each square meter of body area	Plasma volume		
								Total volume, cc	Cc for each kg of body weight	Cc for each kg of ideal body weight		Total volume, cc	Cc for each kg of body weight	Cc for each square meter of body weight
1	64	M	66	79	15.3	35		5890	89	75	3250	3830	58	2110
2	33	M	67	85	17.5	46	5.40	6170	92	73	3220	3330	50	1740
3	62	M	87	69	19.3	47	6.08	7150	82	104	3650	3790	44	1930
4	37	M	75	81	15.6	38	4.80	7080	94	87	3610	4390	59	2240
5	62	M	60	69	16.7	42	5.24	4930	82	71	2950	2860	48	1710
6	68	M	54	53	16.1	35	4.05	5570	103	105	3520	3620	67	2290
7	65	M	73	64	17.2	46	4.78	5950	82	93	3400	3330	46	1900
8	61	M	50	53	14.1	35	4.17	5020	100	94	3280	3260	65	2130
9	53	F	63	61	18.6	56	6.86	5340	85	88	3340	2350	37	1470
10	29	M	62	61	20.0	47	4.58	6040	99	99	3700	3200	51	1960
11	52	M	50	83	14.2	39	4.32	4920	98	59	3155	3000	60	1920
12	37	M	51	67	11.5	34	4.80	5150	92	77	3180	3400	66	2080
Mean value			64.1	68.7	16.5	42.5	5.02	5792	91.5	85.4	3367	3368	54.1	1960
Probable error			2.1	2.1	0.5	1.3	0.16	156	1.4	2.7	46	97	1.8	43.5
Normal values					15.6	42	5.00		87.7		3278		51.2	1920

oglobin in the cell for the group, was 40.9

*Erythrocytes in each cubic millimeter of blood*—The number of erythrocytes for each cubic millimeter of blood varied from 4,050,000 to 6,860,000. The average count was 5,020,000. There were only two cases in which the erythrocyte counts reached 6,000,000, and seven in which they were less than 5,000,000 which is con-

sidered the normal erythrocyte count for each cubic millimeter.

*Hematocrit values*—The percentage of cells by the hematocrit varied from 34 to 56, with a mean of 42.5 which, according to the dry oxalate method, is normal. In five cases, however, hematocrit values were in excess of 45 per cent. This percentage is usually considered normal when the wet oxalate method is used.

TABLE 3

VOLUME OF CELLS AND CIRCULATING HEMOGLOBIN IN CASES OF CHRONIC EMPHYSEMA AND ASTHMA

Case	Total volume, c c	Cells		Circulating hemoglobin		
		C c for each kg of body weight	C c for each sq meter of body area	Total volume, c c	Gm for each kg of body weight	Gm for each sq meter of body area
1	2060	31	1140	903	13 6	499
2	2840	42	1480	1080	16 1	568
3	3360	38	1720	1380	15 9	705
4	2690	35	1370	1105	14 7	564
5	2070	34	1240	824	13 7	494
6	1950	36	1230	896	16 6	568
7	2620	36	1500	1025	14 1	586
8	1760	35	1105	708	14 1	463
9	2990	48	1870	994	15 8	621
10	2837	48	1740	1250	19 9	766
11	1920	38	1235	700	13 9	449
12	1750	34	1100	593	10 6	366
Average	2400	37 2	1394	954 7	14 9	554
Normal values		36 5	1358		14 7	541

*Blood volume and plasma volume*—The mean blood volume for the group of twelve patients was 91 5 c c for each kilogram of body weight (table 2 and 3). The range was from 82 to 103 c c. Marked examples of obesity or of a condition of underweight were not present among the patients. The mean weight was 64 1 kg. If the ideal weight is calculated according to age, sex and height, a mean value of 68 7 kg is obtained, which gives a mean blood

volume for the group of 85 4 c c. In the individual case, the calculation of the blood volume, according to ideal weight, does not indicate that there was a serious deviation in the blood volume except in case 3, in which 82 c c in each kilogram is changed to 104 c c. On the basis of body area, there was a mean value of 3367 c c for each square meter, which is strictly normal.

TABLE 4  
VOLUME AND HEMOGLOBIN CONTENT OF ERYTHROCYTES

Case	Volume index of the erythrocyte	Saturation index, hemoglobin	Volume of the average erythrocyte in c c x 10-11	Grams hemoglobin in average erythrocyte x 10-11	Actual percentage of hemoglobin in the erythrocyte
2	1 02	1 25	8 53	3 24	38
3	0 96	1 10	8 10	3 34	41
4	0 94	1 10	7 90	3 25	41
5	1 10	1 20	9 40	3 91	41
6	1 03	1 40	8 64	3 98	46
7	1 14	1 14	9 60	3 62	38
8	1 01	1 28	8 40	3 38	40
10	1 22	1 29	10 30	4 37	42
Average Normal value	1 05	1 22	8 86	3 64	40 9
(Haden)	1 00	1 00	9 20	3 12	33 9

The plasma volume varied from 37 to 67 c c and the mean value was 54 1 c c for each kilogram of body weight. The range for normal persons is from 48 to 60 c c. In cases 3, 7 and 9, values were below the lower limit of normal. The cases with the higher plasma volumes were those in which there were mild degrees of anemia. The patient in case 9, with a plasma volume of 37 c c for each kilogram of body weight, was not obese, and the blood volume was 85 c c for each kilogram of body weight. This gives a cell volume of 48 c c for each kilogram of body weight as compared with the corresponding normal cell volume of 36 5 c c. This represents relative erythrocytosis due to di-

minished plasma volume. If the plasma volume for the group is calculated according to the ideal weight, a mean value of 48 8 c c is obtained, a value slightly less than normal. According to body area, the plasma volume varied from 1470 to 2290, with a mean value of 1960 c c which is normal.

*Oxygen content and saturation of blood*—Studies of the oxygen content of the arterial and of the venous blood were carried out in seven cases of the group of twelve (tables 5 and 6). The blood was obtained by puncture of the radial or of the brachial artery and was collected under oil.

The oxygen content of arterial blood varied from 18 to 21 8 volumes per



TABLE 5

## STUDIES OF OXYGEN IN THE ARTERIAL AND VENOUS BLOOD IN EMPHYSEMA

Case	Oxygen capacity, volumes per cent	Oxygen content				Utilization in the tissues	
		Arterial blood		Venous blood		Volumes, per cent	Percentage of saturation
		Volumes, per cent	Percentage of saturation	Volumes, per cent	Percentage of saturation		
1	20.5	18.3	89	10.6	51	7.7	37
2	23.5	20.6	87	16.1	68	4.5	19
3	25.9	21.8	84	14.9	57	6.9	26
4	21.0	19.2	91	8.0	38	11.2	53
5	22.4	20.9	93	5.0	22	15.8	70
6	21.6	18.0	83	6.5	30	11.5	53
7	23.0	20.7	89	17.5	75	3.2	13
Average	22.5	19.9	88.3	11.2	49.2	8.7	39.2
Normal values	21	20	95.6	14.5	70	5.5	26

cent, with an average value of 19.9. The oxygen capacity in volumes per cent averaged 22.5, which gave an average percentage oxygen saturation of the arterial blood of 88.3. This indicates a moderate grade of anoxemia, in no case was the percentage of oxygen saturation as high as normal. The lowest percentage of oxygen saturation was obtained in cases 3 and 6, 84.4 and 83.0 per cent, respectively.

The oxygen content of the venous blood varied from 5 to 17.5 volumes per cent, with an average value of 11.2

volumes per cent. The average percentage saturation was 49.2 which is an unsaturation approximately of 50 per cent.

The utilization of oxygen, which is the difference between the arterial and venous oxygen content, showed a wide variation, with an average value of 8.7 volumes per cent (normal 5.5 volumes per cent).

*Studies of vital capacity*—The vital capacity was reduced in cases 1, 2, 4 and 5. In case 7, it was equal to the normal estimated value.

TABLE 6  
VOLUME OF BLOOD, PERCENTAGE SATURATION WITH OXYGEN OF ARTERIAL BLOOD  
AND VITAL CAPACITY

Case	Hemoglobin gm in each 100 cc of blood	Erythrocytes, millions	Cells by hemat- ocrit, per cent	Blood volume		Percentage sat- uration of oxygen of arterial blood	Vital capacity, c c	
				Total volume, c c	C c for each kg of body weight		Actual volume	Estimated volume
1	15.3		35	5890	89	89	3128	4480
2	17.5	5.40	46	6170	92	87	3625	4735
3	19.3	6.08	47	7150	82	84		
4	15.6	4.80	38	7080	94	91	3058	4522
5	16.7	5.24	42	4930	82	93	2911	4255
6	16.1	4.05	35	5570	103	83		
7	17.2	4.78	46	5950	82	89	4149	4000
Average	16.8	5.06	41	6106	89	88.3	3434	4400
Normal values	15.6	5.00	42		87.7	95.6		

#### DISCUSSION OF SIGNIFICANT RESULTS IN GROUP I

The hemoglobin content of the individual erythrocyte indicated 20 per cent more hemoglobin than is found by calculation, according to Haden, for the average normal erythrocyte.

The response of the blood in these twelve cases to the lowered saturation of oxygen was variable. One point is clear, that in no instance did the erythrocytosis develop to a degree to simulate true polycythemia vera. The volume of blood and cells, calculated on the basis of body weight, gave mean values for the group that were very

slightly above the means for normal persons. Probably the difference is insignificant. In only two cases was the blood volume in excess of 100 c c for each kilogram of body weight. In one of these, anemia was believed to be present and the increase in blood volume is explained largely by the increase in plasma. In the second case, with a blood volume of 82 c c for each kilogram of actual weight, and of 104 c c for each kilogram of calculated ideal weight, the percentage of cells by the hematocrit and the concentration of erythrocytes were definitely high. This probably represents

an absolute increase of erythrocytes but not an increase to the degree observed in polycythemia vera. On the other hand, there was evidence of increased concentration of blood as determined by the percentage of cells by the hematocrit and by the number of erythrocytes in each cubic millimeter of blood, this was observed in cases 2, 3, 7, 9 and 10. In only one case (case 9) was this increase of significance, with 6,860,000 erythrocytes for each cubic millimeter of blood, and 56 per cent of cells by the hematocrit. In this case the volume of blood was normal with a diminished amount of plasma for each kilogram of body weight. This tendency to increased concentration without serious disturbance of the volume of the blood and cells for body weight or body area, explains the observations with reference to the individual erythrocyte as determined by calculation.

The studies of the oxygen content of venous blood have shown an unsaturation with oxygen of venous blood sufficient to produce cyanosis. Lundsgaard and Van Slyke have shown that unsaturation with oxygen to the amount of 6 to 7 volumes per cent in the capillary blood is necessary for cyanosis to be produced. The oxygen content of the capillary blood is not known, but probably is represented by the formula  $\frac{A+V}{2}$ , which

2

is the mean between the degree of unsaturation with oxygen of the arterial blood and of the venous blood. When this formula was applied to the seven cases in table 5, cases 3, 4, 5 and 6 had unsaturation values sufficiently

high to produce cyanosis. These criteria for cyanosis do not correlate well with the clinical evidence of cyanosis, but probably this discrepancy can be explained by modifying factors, such as the condition of the surface capillaries and pigmentation of the skin.

Arterial anoxemia determined in terms of percentage saturation, which is the ratio between the oxygen capacity and the oxygen content of the arterial blood, was present in all the cases in table 5. In all of these cases values were below the normal of 95 to 100 per cent saturation. In two cases (cases 3 and 6) low values of 83 and 84 per cent saturation were obtained.

The percentage reduction of vital capacity varied from approximately 33 to 50 per cent of normal.

The correlation of the volume of blood, vital capacity and percentage saturation of arterial blood is shown in table 6. Correlation was not demonstrable between the percentage saturation of arterial oxygen and the volume of blood and cells for each kilogram of body weight. In case 6, with the lowest saturation value, the highest blood volume was obtained, 103 cc for each kilogram of body weight, which if corrected for the ideal weight would be 105 cc and would constitute an example of slight increase in the volume of blood. This increase in blood was not due to an increase in cells but to an increase in plasma which probably was related to the mild anemia.

The data concerning the blood in cases of chronic pulmonary disease stimulate those obtained in experi-

mental work on the dog after evulsion of intercostal and phrenic nerves<sup>s</sup> which was followed by operative destruction of the respiratory function of the diaphragm. Studies on the blood were carried out months after the operation, and significant changes were not noted in the hematocrit or volume determinations. The arterial saturation was low (87 per cent) and the vital capacity was diminished. The results of all laboratory studies were similar to those in the clinical cases.

#### COMPARISON OF RESULTS IN GROUP 1 WITH RESULTS IN GROUPS 2 AND 3

In contrast to the observations in chronic pulmonary disease, attention is called to those in the two cases in group 2, in which polycythemia vera was associated with chronic pulmonary disease (table 7). In these cases, the blood volume was enormously increased and the percentage saturation of oxygen in the arterial blood was markedly lowered.

The remaining case, which, by itself, constitutes group 3 is presented as a probable example of Ayerza's disease, in which the clinical picture is one of extreme cyanosis frequently associated with pulmonary emphysema, hypertrophy of the right side of the heart, marked dyspnea, and secondary sclerosis of the pulmonary artery. In this case, the oxygen saturation of the arterial blood was low and the clinical data correspond well with those given as representative of the syndrome of Ayerza's disease. The blood volume was definitely increased to 114 cc for each kilogram of body weight. The

spleen was not enlarged and there was no difficulty in excluding a diagnosis of polycythemia vera.\*

The average hemoglobin in the individual cell in the cases in group 2 was 34 per cent and in the case of Ayerza's disease (group 3) it was 36 per cent.

#### COMMENT

It has been well established that there are large reserves of erythrocytes in the body that are not in active use in the circulation as oxygen carriers but that can be called into service by various stimulants. Emotional outbursts produce acute transient erythrocytosis. The result is obtained by calling all the available erythrocytes into the circulation and is a question of reserve of erythrocytes rather than of increase in production of erythrocytes.

When animals or man are subjected to a limited supply of oxygen, a similar response occurs. This condition exists at the high altitudes of mountain peaks, in airplane flights at great heights, and by artificial rarefaction at sea level. The effects are immediate and temporary, they persist only after long exposure to these influences.

The limitation of the supply of oxygen in the air may be simulated, in part at least, by conditions within the parenchyma of the lung that serve to decrease the available supply of oxygen to the blood. Patients with chronic pulmonary lesions, if anoxemia occurs, presumably should react in a similar way to that in which persons react who are subjected to long-con-

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\*This case has been reported as a complete study by Constam and Brown.

TABLE 7  
VOLUME OF BLOOD AND OXYGEN SATURATION OF ARTERIAL BLOOD IN POLYCYTHEMIA VERA WITH CHRONIC PULMONARY OR CARDIAC DISEASE

Case	Age and Sex	Hemoglobin, gm 100 c c of blood	Erythrocytes, millions	Blood		Plasma		Percentage oxygen saturation of arterial blood	Comment
				C c for each kg of body weight	Total volume, c c	C c for each kg of body weight	Total volume, c c		
13	56 M	20.7	6.34	168	6360	67	2540	78.0	Polycythemia vera, splenomegaly graded 2, chronic bronchitis, emphysema, cyanosis graded 3
14	43 M	25.6	7.67	185	6160	52	1720	69.5	Polycythemia vera, splenomegaly graded 1, chronic emphysema, myocardial insufficiency, cyanosis graded 3
15	27 F	16.9	4.52	114	7300	59	3790	74.8	Ayerza's disease, emphysema, cyanosis

tinued residence in places where the air is rarefied

With these premises, it seems legitimate to expect that although external respiration may be faulty, either because of anatomic defect or in consequence of limitation in the supply of oxygen, the requirements of internal respiration may be satisfied by an increase in oxygen carrying power

Laboratory and experimental results give ground for statements of general facts which often are not applicable to the complicated conditions present in the illnesses of man. Chronic emphysema, usually complicated by bronchitis, provides a suitable subject for study in this connection. Patients afflicted with this disease are ambulatory, well past middle life, dyspneic on exertion, and frequently when at rest also, they are cyanotic under similar circumstances and have hearts in which degenerative changes are to be expected as the rule rather than as the exception. The pathologic changes within the lung are progressive and unlimited in degree, so that the effort at compensation is long continued, and ultimately fails. The right side of the heart loses competency just as the left side also may lose competency in conditions in which hypertension is produced.

The thin and ruptured alveolar walls, the broken elastica, and the constricted capillaries are characteristic of the disease, and when emphysema is marked, the flow of blood in the lungs is impaired and the patient is comparable to one living for a long period of time at high altitudes with respiratory embarrassment and increased pressure of the pulmonary circulation. The right side of the

heart hypertrophies, then dilates, and dyspnea is followed by cyanosis

#### SUMMARY

In cases of chronic pulmonary disease, chronic emphysema and bronchitis, the response of the blood to arterial anoxemia was variable. Increases in the volume of blood and cells never simulated those found in polycythemia vera. When erythrocytosis was observed, it seemed to be due to changes in concentration, and in only one case was erythrocytosis present to a striking degree. There was an increase in the amount of hemoglobin in the individual erythrocyte. Correlation was not demonstrated between the vital capacity and the degree of arterial anoxemia, or the vital capacity and the response of the blood. Likewise, correlation could not be demonstrated between the arterial anoxemia and the response of the blood. The vital capacity was reduced in some instances to a very significant degree. Cases of polycythemia vera, complicated by pulmonary disease and marked unsaturation with oxygen of the arterial blood, showed the usual excesses in the volume of the blood and cells that are observed in uncomplicated cases of polycythemia vera. In one case of Ayerza's disease there was demonstrated erythrocytosis of sufficient degree to produce significant absolute increases in the volume of the blood and cells.

The clinical observations and the data obtained in this study demonstrate the degree of dysfunction that may take place in respiration before normal reserve is overcome and the collateral function of circulation is called on for compensatory assistance.

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# Treatment of Neurosyphilis\*

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general paresis is entirely halted. However, there is being accumulated a considerable amount of evidence which leads to the belief that a true arrest is obtained. It will suffice for the present discussion, however, to talk of apparent arrest until such time as one has more convincing evidence.

For many decades it has been known that cases of the meningo-vascular varieties of neurosyphilis could be arrested and apparently cured by the use of mercury and iodid. Later, with the use of arsphenamin, an increasing percentage of these cases, whether in the early or late stages, were found to recover with the use of this drug. Whereas, tabes did not give satisfactory results when treated with mercury, arsphenamin produced quite satisfactory clinical and serological results in a small percentage of cases. Serum injections into the subarachnoid space added greatly to the number of cases both of the meningo-vascular and tabetic varieties of neurosyphilis which reacted well. The fact that serological recovery and clinical improvement could be obtained, gave proof that these cases were of the type that could be successfully treated. The problem narrowed down then to a matter of getting a higher percentage of good results.



In cases of general paresis, the problem of treatment presented itself in clearer form. Mercury and the iodids, according to all experience, produced no satisfactory results whatsoever. Arsphenamin, in ordinary dosages, was practically no more effective. Very large doses, often repeated, appeared to give improvement in a small percentage of the cases, but by no means was it conclusively proven that it caused a definite arrest or serological cure in any but rather exceptional cases, nor did intraspinal or intracisternal injections of arsphenaminized serum give conclusive evidence of arrest. Cases of paresis, therefore, offer the ideal material for the evaluation of other methods than those mentioned.

Malaria, as the prototype of febrile therapy, has been used and the results studied for the past ten years. Tryparsamide, a pentavalent arsenical preparation, has been used and the results studied for approximately six years. While these periods are too short to draw any definite and final conclusions, they are long enough to have given us an opportunity to gather a considerable amount of evidence concerning their effectiveness in the treatment of general paresis, and other types of neurosyphilis as well. A conservative summary of the literature of the world concerning the results obtained with malarial treatment indicates that a thoroughly good clinical result is obtainable in about 30% of the cases of general paresis while approximately another 30% show a reasonable amount of improvement. Complete tabulation of the results obtained in the treatment of parietic cases by tryparsamide is not available, but what

information is at hand would indicate that results are substantially the same as obtained by the use of malaria. The important factor to be stressed is that with both these methods, it is possible to obtain complete serological recovery in a considerable number of cases.

The point of serological recovery is extremely important, to my way of thinking. While natural remissions occur occasionally in general paresis, I have seen no evidence to indicate that serological improvement, much less complete serological recovery, occurs spontaneously except possibly in a rare instance where an intercurrent infectious disease has produced febrile effects similar to what are obtained artificially by malaria. In other words, a serological recovery is evidence that the method of treatment used has been effective in producing results which cannot be considered as accidental or coincidental. Wagner von Jauregg, the introducer of the febrile method, and his co-workers, at first laid down the dictum that serological modification was unimportant because cases which showed a degree of serological improvement at times made no definite clinical improvement, and on the contrary, cases showing excellent clinical remissions did not show parallel improvement in the serology. Later studies have, I believe, modified this point of view very materially. Cases that do not show serological improvement are the ones that are most likely to relapse, whereas, the cases which have both clinical and serological recovery are the ones most likely to remain stationary and without relapses.

With malarial treatment serological improvement is quite slow in making

its appearance. In fact, only a slight improvement is usually seen within six months after treatment and it is not until twelve to twenty-four months that the maximum amount of serological improvement is discernible. However, for this discussion I lay great stress upon the point that many cases have now been observed in which, following malarial treatment, a completely normal cerebrospinal fluid has been obtained.

Tryparsamide appears to affect the spinal fluid in a favorable fashion somewhat more frequently and somewhat more rapidly than does malaria. In neither case is it possible to offer satisfactory percentage figures, and one will have to be satisfied with such a statement, as just made, as the best conclusion that can be drawn without substantiating figures. My personal experience has been that it is possible to get a completely negative spinal fluid in a considerable percentage of the cases of general paresis, even including the quite far-advanced cases. In dealing with a group of institutionalized paretics who have been in a hospital for one, two, or three years before treatment was instituted, we have been able in more than 50% of the cases to get a practically negative spinal fluid. Most of this group of cases were quite deteriorated mentally and showed little if any, mental improvement. Physically, improvement occurred and most important the disease did not seem to progress, the mental condition remained stationary, and the patients have lived for a longer period than would be the ordinary expectancy in such cases untreated.

These facts seem to me to offer

definite proof that cases of the most malignant type of neurosyphilis can be arrested or, at any rate, so nearly arrested that no obvious progress of the disease process takes place in the course of several years. I do not believe that it is possible to draw any valid conclusions as to the comparative efficiency of these two methods. They both give relatively satisfactory results in a percentage of the cases, a percentage which is far from reaching 100. Both have certain advantages and disadvantages. The febrile method often works more rapidly, as far as clinical improvement is concerned, than does tryparsamide. At times it apparently fails when tryparsamide succeeds. Febrile treatment is a type of treatment that is fraught with danger, and a small mortality is to be expected through its use. Likewise, it is not available for patients in bad physical condition. The delay in improvement which may be found in the use of tryparsamide, may at times be a definite contra-indication. Tryparsamide will occasionally cause amblyopia and in certain cases, therefore, will not be available. Malaria treatment at times causes arrest in cases that are not doing well with tryparsamide.

It must be emphasized that in the treatment of established cases of general paresis, neither method gives anywhere nearly as high a percentage of satisfactory results as one desires. It is my personal belief that very often the combination of malaria and tryparsamide will achieve a good result when either alone does not accomplish this. This is a point on which there is a difference of opinion, but personal experience has thoroughly convinced

me of the validity of this belief. It is not possible at this time to go into the details of method. I would only state that at times we use several attacks of malaria, as well as other methods of producing fever, with a very long course of tryparsamide aided by arsphenamin and mercury, bismuth, iodids, and at times subarachnoid injections.

Accepting the statement as correct that cases of the most malignant form of neurosyphilis, namely, the parietic, can be arrested, it would seem to follow that the less malignant forms should give us a much higher percentage of success, and this seems to be the case. A very high percent indeed of cases of tabes may be arrested by tryparsamide alone or tryparsamide in conjunction with arsphenamin and intraspinal injections. In the simpler forms of meningeal and meningo-vascular neurosyphilis, the percentage of success now approaches 100%. Of course this does not mean that the degenerative changes can be completely halted nor that sclerotic changes in the blood vessels will be stopped from progressing.

I hope I have made clear that valuable as I consider tryparsamide and malaria and other febrile methods in the treatment of paresis and neurosyphilis, I do not consider them by any means adequate for the treatment of malignant late cases. There are two solutions to be hoped for. First, that we can obtain more efficient methods. Tryparsamide and febrile methods are only indications of the possibility of improvement in the ways and means of treating these cases, and we have every reason to suppose that

in the future more valuable means will be made available.

The second possibility of improving the situation very markedly is the early recognition of central nervous system involvement. The degree of success which we now have with the late and malignant forms of the disorders is evidence that earlier diagnosis followed by our now available methods of treatment will arrest the disease before appreciable damage to the cord or brain has occurred. In the asymptomatic forms of neurosyphilis, the forerunners of clinical meningo-vascular, tabetic, and parietic neurosyphilis, the serological recovery is to be expected in nearly every case. It is only a matter of early recognition and continuation of treatment for a sufficient length of time, then the application of the method which is efficient for the given case. In almost all of the asymptomatic cases, and certainly in the majority of the cases of meningo-vascular and tabetic forms, the febrile method is not necessary. Combinations of tryparsamide, arsphenamin, mercury and bismuth and intrathecal injections will practically always succeed.

Finally, I would call attention to the long-continued treatment that is many times required to produce a serological recovery. It is our usual custom when using tryparsamide to continue it indefinitely and usually without interruption until the desired result is at hand. Having sufficient optimism to believe that a serological recovery is nearly always available, we persevere, however long it may take, week after week, month after month, and year after

year The highest number of trypar-samide injections which we have given to any one patient up to now is 183 injections in a period of little less than five years There is rarely any evidence of cumulative effects or lack of ability of patients to handle the drug

Our present working motto is that a serological arrest, at any rate, is to be expected in practically every case with the methods now available, and it is our problem to use the methods to the best advantage and to continue them until the desired result is obtained



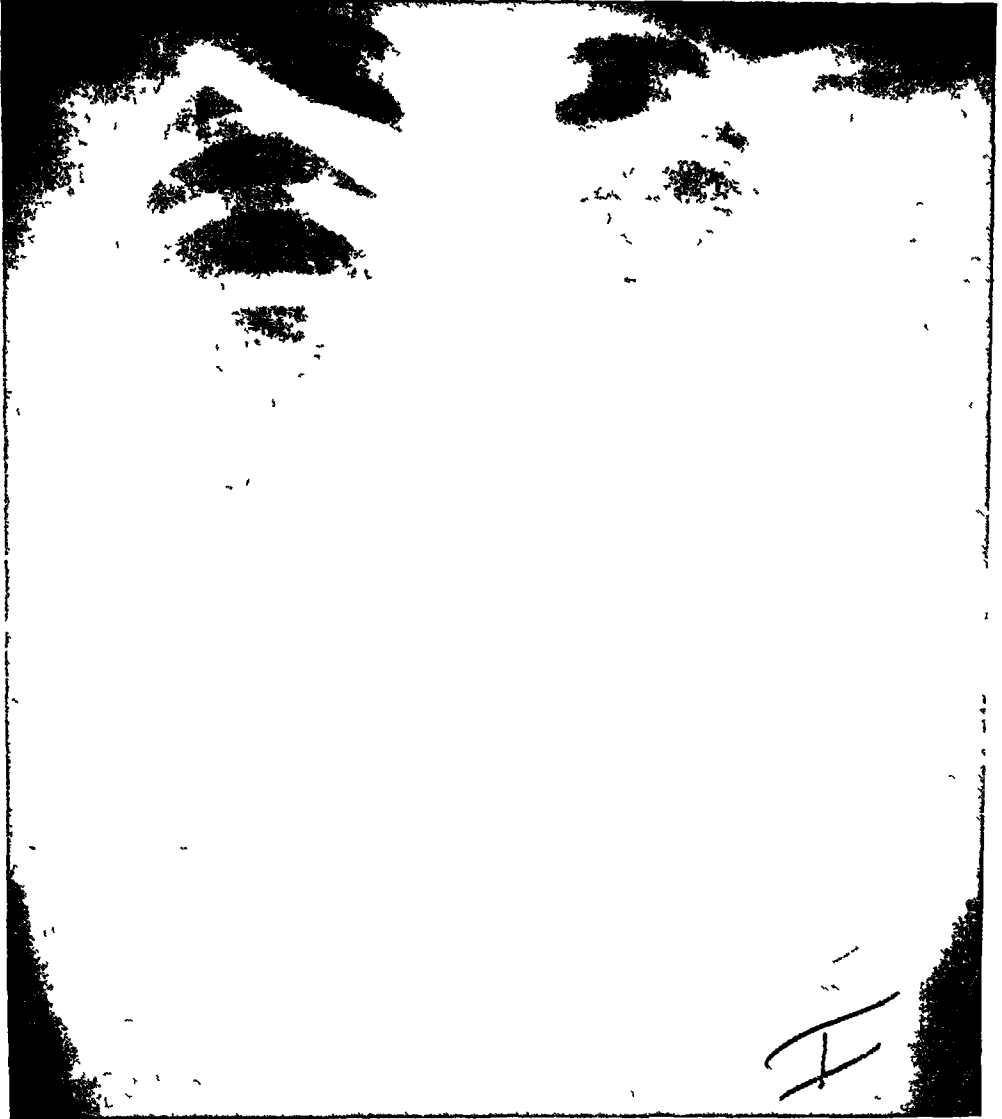


FIG 1 Original plate of chest showing the syphilitic infiltration into the right, middle, and lower lobes (before treatment)



FIG. 2 Same after four weeks of active treatment

mally to light and distance, sclera is normal. The nose is normal. The teeth are in good condition. The tonsils are slightly submerged, but nothing can be expressed from them. The thyroid gland is normal. No masses can be felt. Small glands are palpable in the neck, axilla, and groin. The breasts are normal. The chest is normal in shape. The right side of the chest has a slightly increased dullness at the base anteriorly. The breath sounds are suppressed, no râles are heard. The heart is normal in size, shape, and position. The rate is 85, and the rhythm is normal. Blood pressure is 110/75. The liver and the spleen are not palpable. The extremities and the reflexes are all normal. Abdominal, pelvic, and general sensory examinations are negative. Laboratory data: Urine, negative. Gastric content shows no free hydrochloric acid, microscopic negative. General blood examination, RBC 4,260,000, WBC 7,200, hemoglobin 81%, differential, PMNs 45%, SL 28%, LL 10%, LM 1%, Tr 2%, Eos 4%, no abnormal cells seen. Blood metabolics, blood sugar 0.78%, urea nitrogen 11.3 mg. Four stools negative. Kahn four plus, Wasserman four plus. We were unable to obtain sputum for examination. Electrocardiogram was normal. Because of the findings in the chest and the report from the X-ray examination, a bronchoscopic examination was made and found to be normal. The X-ray examination shows a hard, nodular, homogeneous type of consolidation extending out from the root of the right lung into the right middle and lower lobes, presenting a sharp line of demarcation from the normal lung.

There did not seem to be anything in these films characteristic of a disease that we had ever seen. In comparing these films with those previously taken, we were at once aware that we were dealing with a progressive disease. Because the infiltration had extended, the roentgenologist felt that the most probable condition which this film represented was a Hodgkins disease. Clinically we found no evidence of this disease.

On the following day the Wasserman reports were returned four plus. With this report at hand, we wondered whether or not this might be syphilis of the lung. On consulting with a number of our colleagues we were as much confused as before, because no one consulted had seen a case of pulmonary syphilis, and no one was able to identify the film as such.

We were all agreed that if the patient with a chronic, progressive lung disease showed a marked improvement clinically and by X-ray examination under active treatment for four weeks, we would be justified in making a diagnosis of pulmonary syphilis. The patient was placed under active anti-syphilitic treatment, and at the end of four weeks she showed great improvement clinically, and X-ray examination showed the infiltrated area to be much smaller. We then made a positive diagnosis of syphilis of the lung, and continued treatment. At the present time the patient has no symptoms. X-ray examination shows the chest to be practically normal.

In the medical literature there are probably between two and three hundred authentic cases of pulmonary syphilis. This is interesting in view





FIG 3 Same after six months

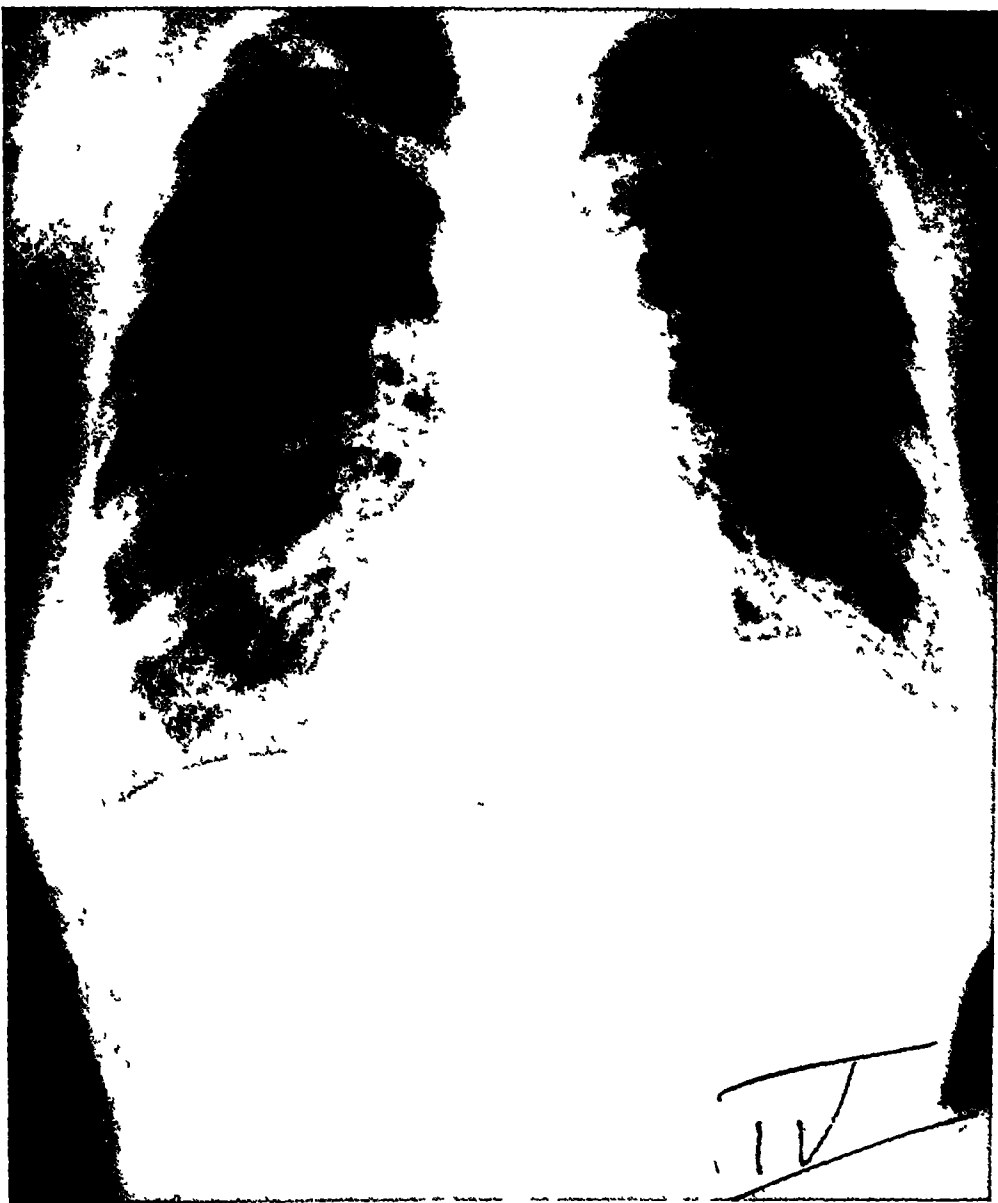


FIG 4 Same after one year's treatment showing almost complete disappearance of the syphilitic infiltration

of the fact that about three per cent of the entire adult population is syphilitic

In 2800 autopsies at Johns Hopkins Hospital, twelve cases of lung syphilis were found. In 4480 autopsies in New York, there were twelve. In 5456 autopsies in California, there were twenty-nine. Fifty per cent of five hundred cases of pulmonary disease in Texas were syphilitic. In Michigan, 78% of 152 bodies showed lung syphilis. In 1300 specimens at the Army Medical Museum no syphilis was found. In the London Pathological museums, twelve. In England, among 100 cases reported to be tuberculous, two were definitely syphilitic. In South Africa, where tuberculosis is rare and syphilis common, 35% of all the natives had a fibroid condition of the lung. In Arizona, in 948 patients with advanced pulmonary tuberculosis, 28% showed x-ray evidence of pulmonary syphilis.

According to Dieulafoy, syphilitic lesions of the lungs are never early. They are probably later than syphilis of any of the other viscera. Save for exceptional cases, it may be said that syphilis of the lung appears only in the advanced tertiary stage of the disease. The interval between the primary infection and the development of the lung lesion varies between one and twenty-five years. The average is ten to eleven years. The ratio of lung syphilis to visceral syphilis is roughly one to twenty.

Kaisner states that there is no definite picture of pulmonary syphilis. However, many observers state that the presence of plasma cells particularly about the blood vessels and bronchi, are characteristic of lung syphilis. The

finding of spirochetes is unusual. Our Dr. Warthin is outstanding in that he is one of the few who has demonstrated their presence in the lung tissues.

Chesney has shown in his experimental work in rabbits how fibrous tissue favors the growth and development of spirochetes.

The pathology of pulmonary syphilis is similar to that of pulmonary tuberculosis. The acute and the chronic types of the disease are found. In the chronic type, miliary gummata may be present and increase in size and number until consolidation exists. Organization may occur or progress to softening with abscess, cavity formation, gangrene, or fistula, rarely to calcification. Fatal hemorrhages may occur. Regeneration of connective tissue may be present, especially about the bronchi and the vessels, or be massed, producing a lung cirrhosis with great deformity and possibly bronchiectasis and pleurisy. Large single gummata are rarely found. Microscopically mononuclear leucocytes and plasma cells are said to be frequently found in syphilitic scar tissue. Syphilis of the vessels of the brain and the aorta, testicles, bone, skin, and amyloid changes are most frequently associated with lung syphilis. Pulmonary tuberculosis is associated in from 3% to 11% of the cases of pulmonary syphilis.

The acute form with a sudden onset of fever, weakness, cough, with or without expectoration, dyspnea, weakness, and sweats, has been described, but it is not common. The chronic form of pulmonary syphilis with a slow, insidious onset, in course re-

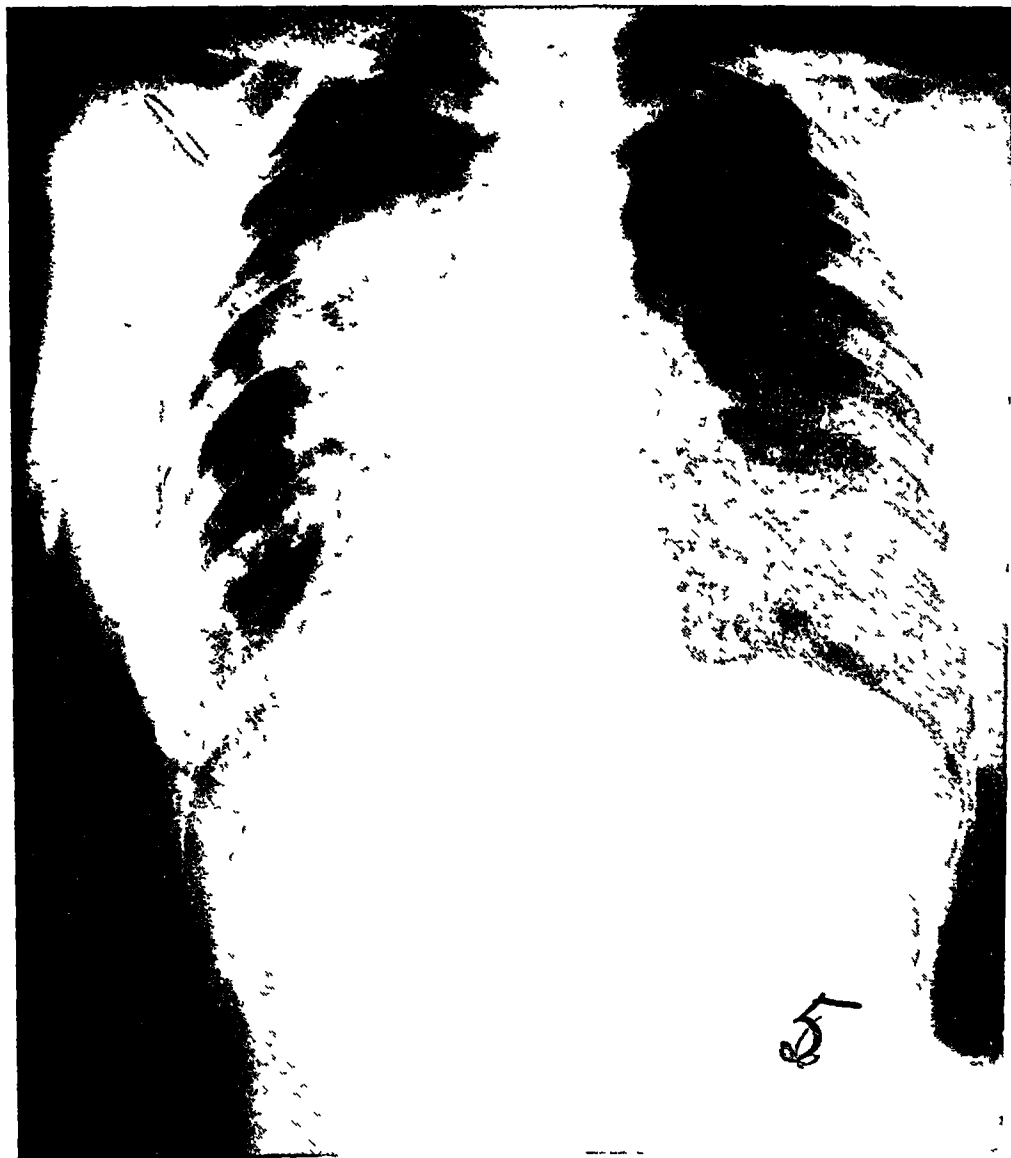


FIG 5 Hodgkins Disease Original plate of chest showing Hodgkins infiltration into left lung

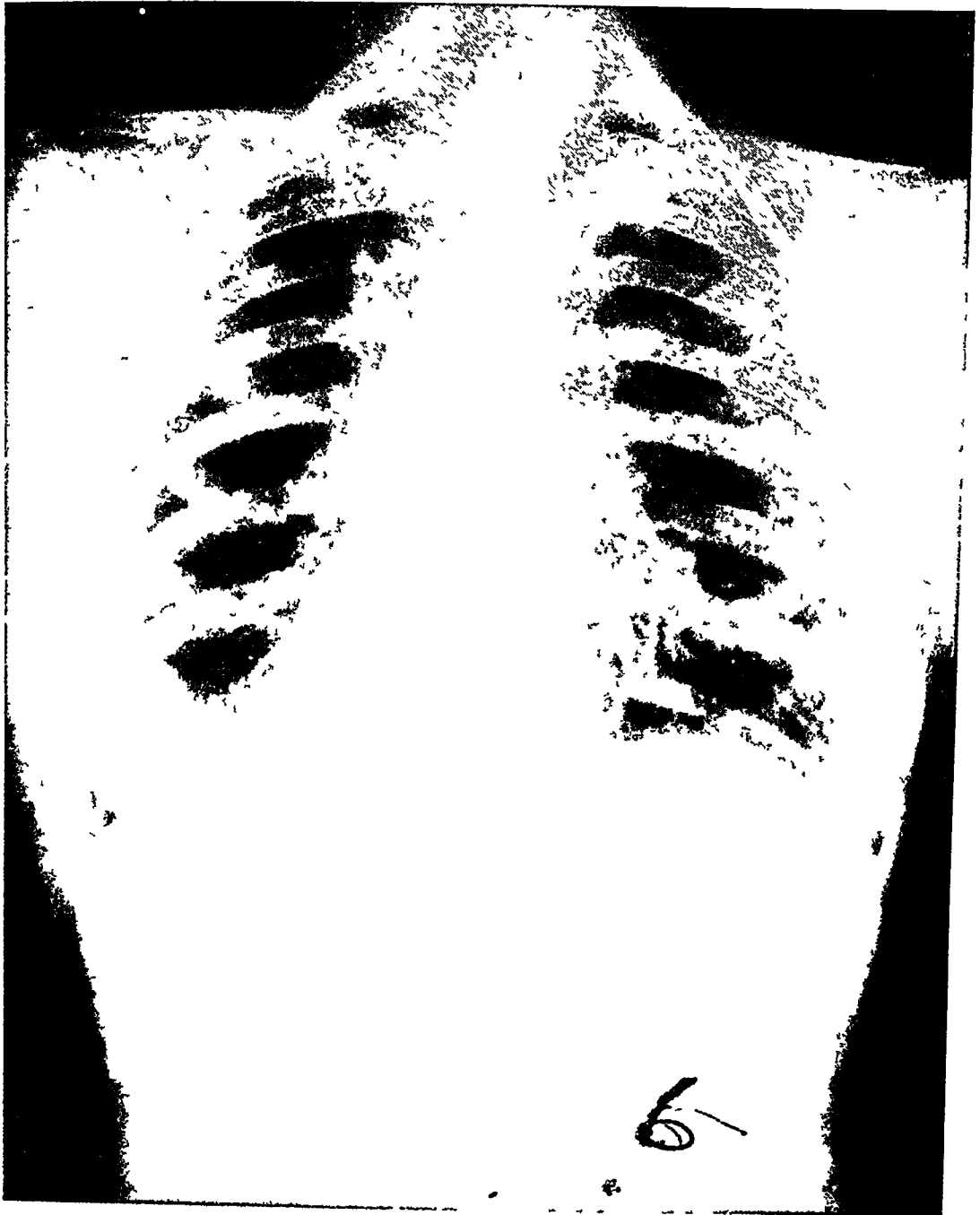


FIG. 6 Same as Figure 5 after X-ray treatment

sembling a chronic tuberculosis, having very little fever, weakness, loss of weight, cachexia, and dyspnea out of proportion to the physical findings is similar to our case and the form most commonly met with in medical practice. The chronic forms with softening abscess, and gangrene, are like the tuberculous varieties. The bronchiectatic type is not different from any bronchiectatic disease. The physical signs simulate those found in pulmonary tuberculosis, varying according to the existing pathology. The spirochete has not been found in the sputum. The Wasserman is positive in more than fifty per cent of the cases. X-rays usually show a unilateral infiltration involving the middle and lower lobes, beginning near the hilus and extending peripherally.

An individual complaining of symptoms referable to the chest with dyspnea, in whom the physical and X-ray examinations of the onset show a unilateral lower lobe lung disease, a positive Wasserman, with or without other forms of syphilis, and a negative sputum should be diagnosed as having a pulmonary syphilis. Tuberculosis, sporotrichosis, aspergillosis, blastomycosis, pulmonary distomatosis, cysts, tumors, and Hodgkins disease should be considered in making a diagnosis. The prognosis of early lung syphilis is good unless the syphilis of some other part, as the brain or vessels (aneurysm) is too far advanced. Then the prognosis is not good. The usual vigorous anti-luetic treatment should be used with frequent physical, blood, urine, and X-ray examinations.

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# The Need for Emotional Data in the Medical History\*

By JOHN FAVILL, A B , M D , F A C P , *Chicago, Illinois*

THIS paper is a neurologic plea to internists to make, as a routine procedure in all medical histories except those of acute infections, some definite inquiry about possible disturbing emotional factors. By the latter I of course do not mean so-called unconscious matters which belong to the orthodox psychoanalyst. Neither do I suggest any intensive "third degree" probing by a junior intern who takes histories. But I am certain that many cases could be saved much delay and expense were the opportunity offered them early to state the existence of painful memories, present dilemmas or fears regarding the future.

Two conditions are necessary for the obtaining of such data. First, the patient must be convinced that it is relevant and may be important, second, the patient must be impressed with the truthworthiness of the questioner and the institution he may represent. It is obvious that these conditions cannot always be fulfilled. An attempt to meet them however, would certainly yield more results than the lack of any such attempt, and even a failure would prevent a given func-

tional patient from subsequently criticizing the doctor or the hospital for never having asked about what later proved to be the chief source of difficulties.

This is not the place and I am not the person to prove any theory of the emotions. But I will state a practical viewpoint for human beings with some simple examples. I think of awareness as a mystery which each of us carries and which I cannot explain. In it appears a sensation such as pain due to a nerve impulse initiated by an external pin. A thought follows "It is a pin in the back of the chair." So far there is little if any emotion. But, on turning around, an unruly child is seen grinning with a pin in hand. A new thought comes "That child ought to be spanked." This starts anger. Or, again, a sensation of pain appears as the result of an internal wave of peristalsis. The first thought, "It is those baked beans I ate for lunch," causes no particular emotion. But remembering a recently read medical article brings the thought "It is the lower right side and may be acute appendicitis." This easily lights a fire of fear. Finally, a person expectorates something bloody into a wash bowl. If he has had a tooth extracted an hour be-

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\*Written for the meeting of the American College of Physicians, Boston, Mass., April 10, 1929 but not read.

fore, there is no emotional disturbance. If, however, he has had no obvious cause for it but has been having bronchitis for months and the expectoration followed a cough, then the quick stream of ideas of tuberculosis, Arizona, interrupted career and death produce almost instantly an emotional state which may be acute.

Thus emotion appears to be a result of certain thoughts, somewhat as a sensation is the result of certain stimuli. The thoughts need not be in any language, they may be visual or other images with concepts of relationship or causality or potentiality, but I feel sure that some such awareness of a situation must precede the phenomenon we call emotion.

What follows the emotion is an individual affair. Effects will sometimes show in the endocrine, sometimes in the vegetative, sometimes in the voluntary motor system. I cannot consider these effects as part of the emotion itself.

Such effects are, however, undeniably the cause of many and various symptoms. Prominent among them are pallor, blushing, pylorospasm, cardiospasm, vomiting, diarrhea, syncope, precordial pain, palpitation, sweating, polyuria, tremor, dry mouth, dilatation of the pupils, and sense of impending death. These symptoms are often the causes of new emotional disturbances. A vicious circle results. A simple example of this sort is illustrated by the following case.

T. C., male, aged 27, married, was seen December 19, 1928, complaining of slight pain in the top of his head, a sensation of something coming up from the stomach, and sweating hands.

These symptoms had been occasionally present for several years, but now were coming in short attacks occurring many times a day. He feared death during most of them, and felt unable to continue his work as a clerk. He stated that he had been to at least seventy-five doctors, most of whom had examined his heart at his request and found nothing wrong. On inquiry, I found his first attack had occurred four years previously when he was hanging by both hands onto the rear of a crowded street car. He feared he would fall off but did not. The second attack occurred one year later and in it he noticed palpitation. (His position in the first attack would have prevented his noting this.) Other attacks came with gradually increasing frequency. He admitted that fear of death was the worst feature of the attacks. It was explained to him that the first one might have been a palpitation from some unimportant cause but which became the starting point for a severe fear reaction. Search for causes of palpitation revealed no organic disease but there was a history of excessive coitus, excessive tobacco chewing and cigarette smoking, at least four cups of coffee daily and the habit of bolting his meals whether hurried or not. He accepted the explanation after some hesitation and agreed to change his habits. He stated that not a single one of the seventy-five physicians previously consulted had made any inquiry along these lines or any similar suggestions. He has continued to work and not returned for further treatment.

In my experience a very distinct majority of cases having this general



type of disturbance have not buried the data in the unconscious. At least sufficient data is available in the majority to permit a procedure leading to a satisfactory adjustment. This procedure includes first, correcting erroneous beliefs about symptoms, diseases, etc., second, bringing to the patient an understanding of the chain of events, and third, encouraging him to form new reaction habits. Among the factors determining the result, on the part of the patient, are constitutional defect, age, severity of disturbing factors, intelligence and cooperation. On the part of the physician there is need for intelligence, unfailing patience, and sincerity.

The neuropsychiatric brotherhood has appreciated the importance of these matters for many years. The body of internists seems often to have been either impatient or neglectful or ignorant of them. It is only two years since the chairman of the section on medicine of the American Medical Association gave as his address "Psychic and Emotional Factors in General Diagnosis and Treatment,"<sup>1</sup> which was followed in the same session by a series of papers on phases of this problem. I have looked through a number of books and manuals on history taking and found little of what I want to propose. The *Clinical History in Outline*<sup>2</sup> gives a single line, "Psychic disturbances: shock, worry, grief." The *Examination of Patients*<sup>3</sup> makes

no definite suggestion. "History Taking and Recording,"<sup>4</sup> does refer the user to Kirby's<sup>5</sup> excellent manual, but in itself gives only the words "Emotional State" in two places. A more satisfactory suggestion occurs in Dock's "Outlines for Case Taking,"<sup>6</sup> consisting of this list: repressed desires, moral or physical shock, business cares, over-exertion, fright. This occurs, however, only in the section for diseases of the nervous system.

For some years I have been using a certain skeleton framework for history taking and the teaching of it which has the advantage of lessening the burden on memory and of presenting a complete scheme of arrangement of data. A mere glance at it often suggests lines of inquiry which otherwise would be forgotten and the place of each item is made obvious. (See Fig. 1.)

The division by systems, usually limited to the physical examination if used at all, is here carried back through the complaint and forward through the end result. The letters across the top refer to Complaint, Present Illness, Past History, Habits, Family History, Examination, Laboratory, Diagnosis, Treatment and End-result. The systems at the left are self-explanatory except for the fifth which means 'Blood, Lymph, Endocrine and Unclassified'. The numbers are merely

<sup>1</sup>James A. Corcoran, Paul B. Hoebler, New York, 1926, PP. 28 and 52.

<sup>2</sup>Geo. H. Kirby, "Guides for History Taking and Clinical Examination of Psychiatric Cases," N. Y. State Hospital Commission, Albany, 1921.

<sup>3</sup>George Dock, Geo. Wahr, Ann Arbor, Mich., 1921, P. 34.

<sup>4</sup>R. P. Woodvatt, Jour. A. M. A., Vol. 80, No. 13, Sept. 24, 1927, P. 1013.

<sup>5</sup>P. G. Wooley, C. V. Mosby Co., St. Louis, 1916, P. 29.

<sup>6</sup>Nellis B. Foster, W. B. Saunders Co., Philadelphia and London, 1921.

SYSTEM	C	PI	PH	H	FH	E	L	D	T	RES
Circulatory	1	11	21	31	41	51	61	71	81	91
Respiratory	2	12	22	32	42	52	62	72	82	92
Alimentary	3	13	23	33	43	53	63	73	83	93
Urinary	4	14	24	34	44	54	64	74	84	94
B L C etc	5	15	25	35	45	55	65	75	85	95
Reproductive	6	16	26	36	46	56	66	76	86	96
Skeletal	7	17	27	37	47	57	67	77	87	97
Tegumentary	8	18	28	38	48	58	68	78	88	98
Nervous	9	19	29	39	49	59	69	79	89	99
Mental	10	20	30	40	50	60	70	80	90	100

Fig 1 Chart showing 100 possible divisions of a complete systemic medical history record

for paragraphing purposes. Even they are easily remembered since in a given system, such as Alimentary they always end in the same digit 3-13-23 etc. A given part of the history, such as Habits, is covered by one decade, 31-32-33 etc to 40. The lists of items possible for recording or inquiry under each number are quite debatable but I have worked out what I believe is a fairly satisfactory series of lists which I hope to offer for consideration at a future date. It must not be thought that I expect such a framework to be often completely fulfilled. Its use however as a reference system for thinking I believe is well justified.

The present suggested inquiry falls under paragraphs 10-20-30-40-50. This means Complaint, Present Illness, Past History, Habits and Family History—all in regard to mental items, somewhat as follows:

Par 10 Complaint, if not forthcoming may be covered by a simple

question such as "Have you noticed anything different recently with your memory, thinking power, concentration or emotional balance?"

Par 20 Present illness, if any, will be taken practically in patient's words.

Par 30 Past history is the crux of my whole discussion. I suggest that the history-taker use a fairly definite formula, varied when necessary to suit the intelligence of the patient as follows: "We realize now that many sicknesses are made worse by worry and fear and too much thinking and I must ask you to tell me whether you have had any mental or emotional distress from any cause. I will read you a list and ask you to say 'Yes' or 'No' to each. You need not give any details unless you wish.

Financial strain

Business problems

Legal complications

Social difficulties

Domestic or sexual difficulties

Religious difficulties

Fear of future events or acts

Fear of disease, physical or mental

Any undecided problem or conflict

Past shocking experience

Past grief or disappointment

Unspecified "

Par 40 Habits reading, study, rest, religion, recreation, hobbies, etc

Par 50 Family history of any "nervous breakdowns", eccentric characters, epileptic, defective, alcoholic,

drug-using, insane or lawless individuals

The obtaining of significant data, especially under Paragraph 30, calls for a consultation with the neuro-psychiatrist

It seems to me that the use of this procedure in a medical service gives the intern valuable experience when the patient cares to talk freely, gives the patient an easy first step in unloading worry, and greatly betters the chances for catching mental elements early and dealing with them effectively

# Factors in the Prognosis of High Blood Pressure\*

By W W HERRICK, M D, *New York City*

WHEN discussion is undertaken of the prognosis or treatment of any pathologic state, the etiology of which is unknown, difficulties are at once met. To this rule arterial hypertension is no exception and more than one competent observer has stated that its satisfactory prognosis cannot be made. Such an attitude of avoidance, while safe, is for the clinician most unsatisfactory and in certain kinds of practical work intolerable. Is it necessary? It is the writer's opinion that experience has reached a point at which one may profitably attempt to set down in a concise way what has practical bearing on this difficult subject. One may use the philosophic method of approach, attempting to understand the fundamental nature of high blood pressure and from such a basis to reason its consequences, or the method of experiment—the study of the experience of others or of one's self in dealing with this malady.

From the viewpoint of physiology there appear to be two chief factors in high blood pressure, i.e. cardiac output and peripheral resistance. Of these the peripheral resistance seems the factor of dominant clinical im-

portance. Through the sensitive vasomotor system, this peripheral resistance may be influenced by mechanical, chemical, nervous, endocrine, and other factors. However, until the physiologist gives more complete knowledge of the sympathetic nervous system and of the glands of internal secretion, the clinician must work under the handicap of partial and very limited command of essential facts in the etiology of high blood pressure.

Like other symptoms, hypertension may be associated with a variety of conditions. Chief among these are increased intracranial pressure, physical and emotional stress, aortic insufficiency, renal insufficiency, thyroid disorders, the action of such substances as adrenalin, pituitrin and ephedrin, certain toxemias of pregnancy, and some types of arteriosclerosis, in at least one of the last named, probably more as cause than effect. Since we are dealing only with prognosis, we can dismiss these types of what may be called secondary hypertension by the general statement that their outcome is that of the associated and underlying condition. This leaves for consideration from the standpoint of prognosis the great group of primary or essential hypertomias, so called because in it we cannot as yet find any associated or apparently causative condition.

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\*From the program of the Boston meeting of the American College of Physicians, April 11, 1929.

While our limited knowledge undoubtedly lists under the title essential hypertension conditions of varied etiology, most of the cases run true to type. In their physical characteristics, the patients are usually thickset and stocky, deepchested with broad hips and shoulders, short necks and round heads. They are likely to have thick skin, abundant and often heterosexual distribution of hair. Mentally they are serious, earnest, conscientious, enthusiastic at work, at their infrequent play, and too often at table. They are usually successful and, as Moschowitz aptly says, they often "die of success." Of great interest is the remarkable resistance of this group to both major and minor infections. Because of the intensity with which they carry on, many of the world's leaders are found in this group. Rarely a thin, angular type will display a hypertension which seems to fall under the definition of essential hypertension. The striking variation from the dominant type suggests that further study may reveal differences in etiology.

Can any satisfactory approach be made to the problem of the etiology of essential hypertension? Health is as dependent upon equilibrium of function as upon integrity of structure. Because of the difficulties in estimating function, too great emphasis has been placed upon structural changes in our definition and study of disease. Essential hypertension seems to be one of the few disorders in which an initial functional imbalance reveals itself long before changes in structure can be found.

The earlier view of Gull and Sutton, furthered by Romberg and others

that hypertension is secondary to a narrowing of the arterioles from arteriocalillary fibrosis has been largely superseded. The weight of competent opinion now holds that the high blood pressure precedes and probably causes the secondary changes in the vascular system. These changes are most pronounced and characteristic in the arterioles. Fishberg states that they consist in an irregular deposit of hyaline material directly under the endothelium, later undergoing lipid change. In the larger arterioles there is hyperplasia of the internal elastic membrane with reduplication and formation of lamellae. Regressive changes follow with the appearance of hyaline and lipid substance and a proliferation of connective tissue. The result is a narrowing of the lumen or obliteration. Fishberg further states that there is a progressive atrophy of the muscle cells of the media with hyaline and fatty changes and finally fibrous replacement rather than the hypertrophy more commonly described.

This same observer finds that these changes are by no means universal. The small interlobular arterioles and vasa afferentia of the kidney were found involved in 100% of the 72 cases examined at necropsy and the changes were more advanced here than elsewhere. Involvement of the arterioles of the spleen, pancreas and brain follow in this order of frequency. The vessels of the heart in essential hypertension show changes with surprising infrequency, those of the lungs, muscles and skin are almost unscathed.

If the concept of a primary functional vascular disturbance character-

ized by exaggerated vaso-constrictor tendencies with later and consequent organic changes in certain selected parts of the vascular tree be accepted, closer inquiry may well be made into the features of the earlier or functional stages that are capable of clinical demonstration. O'Hare and others have already called attention to this phase of hypertonia. O'Hare found the vasomotor system in hypertension very labile and sensitive. Excitation and exercise usually caused a marked and abrupt rise. The vessels in hypertonia were found extremely sensitive to adrenalin, very sharp rise in blood pressure taking place immediately after injection of this substance in the muscles.

The functional disturbances usually believed to be somewhat characteristic of this malady are

- 1 An ill balanced personality already described with the chief tendencies pressure of activity and overearnestness

- 2 Tachycardia, at first periodic, later more continuous

- 3 Flushing

- 4 Headache—often migrainous

- 5 Vascular crises—usually episodes of mild anginoid pain, anxiety, palpitation or tachycardia with rise in blood pressure

- 6 Undue or prolonged rise in systolic and diastolic pressure in response to emotion or effort

To glean anything of prognostic value from study of such evidences of disturbed function is indeed difficult. The most tangible of these seems the rise in pressures following effort or emotion. Study of this and the pulse rate simultaneously gives certain data

which can at least be expressed mathematically and may have some value.

One of the methods used in estimating the functional response of the circulation is the simple exercise test. Subjects' blood pressures and pulse rates are recorded while at rest. Exercise is then given to the point of beginning dyspnea when records are again made. Observations are then taken every minute for five minutes while the subject lies at rest.

No attempt has been made to make the test mathematically exact by having subjects of the experiment perform a measured amount of work. It is quite impossible to adapt such a test to all phases of circulatory disease, especially those in the advanced stages. A more universally satisfactory test for all types of cases seems the performance of enough work to bring about moderate dyspnea. This might be running up two flights of stairs for a youth in normal health or but a few liftings of the hands above the head for the bed-ridden patient with impending circulatory failure.

Study has been made of the response to an exercise test of this kind of normal individuals of different ages and of examples of hypertensive cardio-vascular disease. The latter have been divided into those in the early phases of the malady when no organic changes in the circulatory system were demonstrable, (Phase I), those with slight or moderate changes, (Phase II), and those advanced (Phase III) or terminal cases, (Phase IV), showing marked or extreme structural damage.

Without giving too much detail either in text or chart the results of

this study may be given schematically in Chart No 1

In harmony with the findings of Barath and others, it is apparent that in Phase I, the youthful normal, we have the ideal state of the circulation. In response to effort causing dyspnea, there is a moderate rise in systolic and a slight but definite fall in diastolic pressure. This results in a rise in pulse pressure which expresses the increased stroke volume output of the ventricle and a peripheral relaxation in response to the call for increased supply of blood to meet the demands of effort. The return to the previous or a lower level is prompt.

In Phase II we have the typical response of the individual in middle life or of one in early life with a beginning hypertonia. The rise in systolic pressure is more marked and the sub-

sequent fall is less prompt and rarely to a lower level at the end of five minutes. Even in this early period of circulatory disorder the diastolic pressure is notably affected, tending to rise and to remain higher for some time after effort.

In the examples of established hypertension with slight or moderate structural changes in the vascular system, (Phase III), one meets the widest fluctuations in blood pressure in response to effort causing dyspnea. In some the changes in systolic pressure are extreme. The fall in systolic pressure is tardy and often at the end of five minutes the reading is above that of the previous resting level. The diastolic pressure in this phase is less variable. It may rise, but in my observation almost never falls as a result of effort.

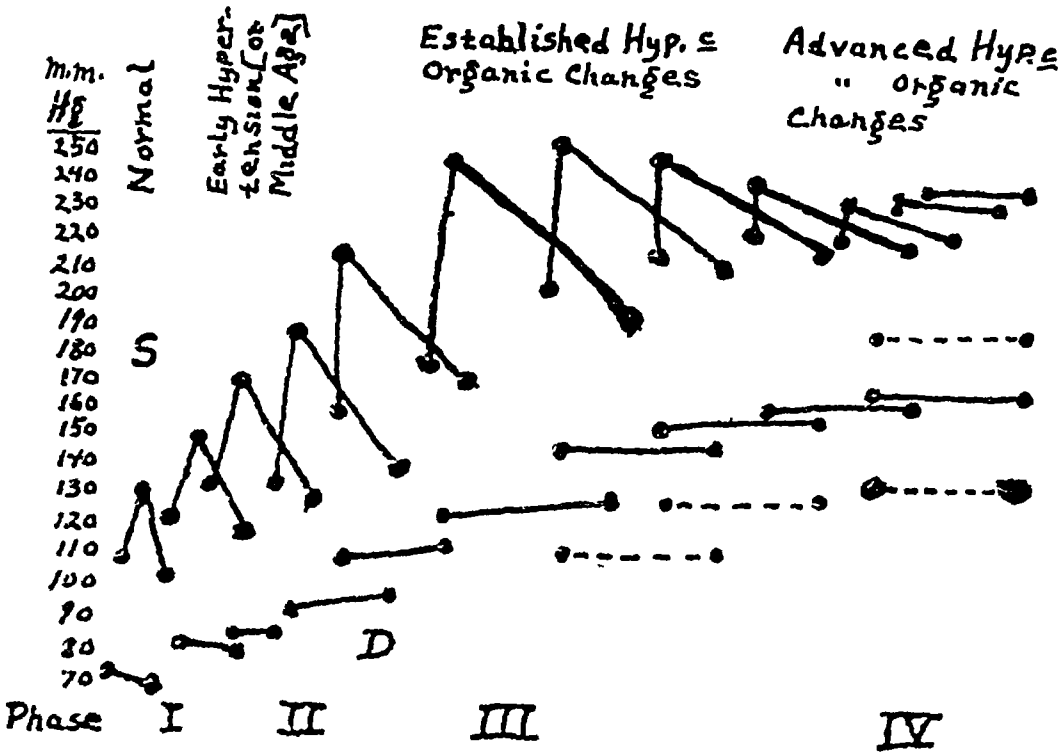


CHART I

In the last group, (Phase IV), a very interesting fixation of both systolic and diastolic pressures is met. In this group are placed those who show marked arterio-sclerotic changes in retina, kidney or elsewhere in the vascular tree of a kind associated with a poor prognosis. We observe a fixation of both systolic and diastolic pressures at high levels with no variation as the result of exercise. Impression is that the circulation has been extended to the limit of its functional capacity even in conditions of repose and has no reserve by which it can increase its output to accommodate effort. It may be said that this type of response or the lack of it is found only in those showing the most extreme structural alterations in the vascular apparatus.

It is realized that observations of this kind are very rough and inexact, that there are plenty of exceptions to any rule in clinical work. Conclusions, however, are based upon a large number of observations chiefly from office practice made over a period of several years. It is believed that the functional response of the blood pressure to effort can be correlated with the degree of organic changes of the kind to be described in the second part of this paper in a manner that has some prognostic value.

Cases with a persisting fall in systolic pressure with a maintained or rising diastolic pressure are of serious import and indicate a weakening myocardium. In such, an added and not infrequent factor in an unfavorable prospect is a pulsus alternans.

## ORGANIC FACTORS IN PROGNOSIS

These have the greatest value. They are always present in any case of long standing or of fixed and marked hypertension. Upon their presence seems to depend the onset of the symptoms we associate with the more advanced phases of the malady under discussion.

1. CARDIAC FACTORS. These center about the functional efficiency of the myocardium. We know from the studies of Janeway, Allbutt, Paullin, Spiunt and others, that the majority of those with essential hypertension die a cardiac death. The most ominous condition in prognosis is that of congestive heart failure or circulatory stasis. Cases with this end result of hypertension and arteriosclerosis usually present a declining systolic and a lowered pulse pressure and, although they may rally for a time with proper management, the end is seldom far away. Auricular fibrillation following hypertension is usually of serious import. While I know of no statistical study on the point, experienced clinicians agree that angina pectoris when associated with high blood pressure, although always serious, does not carry with it the grave prognosis experience justifies in cases with normal or low pressure. It is possible that the greater vaso-motor instability of the patient with essential hypertension leads to the angiospastic type of angina which is less serious than that associated with the coronary sclerosis of a decrescent type, more often found in cases with normal pressures. Study of large groups of these two types of angina from the viewpoint of prognosis is needed.



*VALVULAR DEFECTS* a Mitral stenosis Not infrequently this lesion of rheumatic origin is associated with hypertension. These patients seem to carry the lesion with comparatively little embarrassment from the hypertension. Perhaps the organization of the mitral valve prevents the development of the relative mitral insufficiency which is such a common feature of advancing hypertonia. The integrity of the myocardium is here the chief prognostic factor.

b Mitral insufficiency when due to stretching of the mitral ring and attended by great enlargement of the left ventricle is always ominous. When there is no demonstrable dilatation of the left ventricle and the circulation is well maintained, a mitral systolic murmur may be passed over with the reservation that it may be a prophesy rather than a sign of weakened musculature of the ventricle. The cardiac capacity is the decisive point in prognosis.

c Aortic insufficiency When featured by a low diastolic pressure and a high pulse pressure this lesion in the presence of hypertension usually presages early disaster. This may follow sudden or gradual cardiac insufficiency or an anginal episode. Syphilitic cases with aortic insufficiency and hypertension must always be viewed with great concern. Those having rheumatic or other non-luetic etiology may carry on much longer. The myocardial capacity is again the final arbiter. The diastolic murmur is usually very loud and distinct in cases with low diastolic pressures. The examples of aortic insufficiency with normal or high diastolic pressures in

the presence of hypertension usually reveal a very soft, barely audible diastolic murmur over the sternum. The origin of this murmur is probably in a very small defect in the mechanism designed to close the aortic orifice—either a slight stretching of the aortic ring or a slight retraction or rigidity of one or more cusps. An aortic insufficiency of this kind does not carry much weight in prognosis and for practical purposes can be almost ignored.

d Aortic stenosis is a lesion of the elderly and, while it always presents the threat of a gradually advancing insufficiency of the left ventricle, may exist for many years with little progress. It is not often associated with hypertension.

2 *THE ELECTROCARDIOGRAM* This has some importance in the prognosis of the myocardial changes following hypertension. Its value, however, is easy to exaggerate and it is of much less weight than the results of other methods of examination. When there are significant disturbances in the P-R time in the QRS complex or T wave, a bit of valuable confirmatory evidence is brought out. Apart from collateral facts, this may be unreliable for any final judgment and should always be subject to strict clinical control.

3 *THE PERIPHERAL CIRCULATION* b The large vessels. The aorta may be examined by ordinary physical methods or by the fluoroscope. Owing to the emphysema so often present in states of hypertension, the former methods are less reliable than direct visualization with the roentgen ray. The slight prominence

of the aortic knob at the junction of the transverse and descending aorta has little prognostic significance. Widening of the entire aorta with undue pulsation is only present in cases with extensive changes in the circulation. According to Sprunt such have a serious prognosis. Diffuse enlargement of the aorta, prominence of the aortic knob and dilatation of the descending aorta—all frequent in arteriosclerosis—are often mistaken for aneurysm by the inexperienced. Especially should one be wary of placing such an interpretation upon the bulging of the descending aorta just above the diaphragm. Physical evidence such as dullness beneath and beside the manubrium, undue pulsation here and in the episternal notch or a rough systolic murmur over the aortic area are usually present when there is significant variation from the normal. The non-syphilitic aortitis can usually be distinguished from that due to lues. Luetic aortitis is relatively rare in patients over 50 whereas the decrescent type is a feature of late middle or advanced life. In the syphilitic cases lengthening and bowing of the aorta and a tendency to sacculation is characteristic, aortic insufficiency with low diastolic pressure is more common, symptoms of circulatory disturbance more severe and the clinical and serological proof of syphilis usually obtainable.

Of the larger peripheral vessels those accessible to the examining finger are the brachials, radials, temporals, abdominal aorta, femorals, popliteals, internal malleolals and dorsales pedes. The brachial vessels are most readily palpated. The blood stream should be

obliterated by pressure above and the character of the arterial wall estimated distal to the point of obstruction. Thickness, tortuosity and beading are the qualities of most significance. Changes of this kind in the larger arteries have little prognostic value. In persons used to manual labor, sclerosis of the large vessels of the extremities does not appear to influence length of life. Changes in the large peripheral vessels may be found as often with as without hypertension. These conditions seem not to have very definite relation. This is quite in contrast with the small vessel sclerosis as shown clinically in the retinal circulation. It is very exceptional that any well marked retinal arteriosclerosis is not attended by high blood pressure of long standing.

One type of hypertension needs emphasis. It has been well described by Fineberg. This is seen in the elderly with well marked sclerotic changes in the larger peripheral vessels and the aorta and with little or no apparent sclerosis of the smaller vessels as judged by ophthalmoscopic study. The peculiarity of the blood pressure is an elevated systolic and a normal or low diastolic reading. The left ventricle is almost always much hypertrophied and a relative mitral insufficiency frequent. The hydrodynamics of this type of hypertension seems to be the large stroke volume output of the hypertrophied left ventricle into a relatively rigid arterial tree and without undue vasoconstrictor influences. The disturbance is mechanical rather than functional, the changes are decrescent and largely primary rather than secondary. The usual ending is in cardiac

insufficiency Evidence of the arteriosclerotic kidney is often found Cerebral hemorrhage is infrequent Cases of this kind have a comparatively good prognosis and may carry on for years

(b) The Smaller Vessels, Although it is known that sclerotic changes may take place in one vascular field and not in others, much of general application may be inferred from the discovery of important local vascular pathologic changes Especially in a condition in which the antecedent functional disturbance affects the circulation so universally, can the secondary vascular sclerosis when manifest in one series of vessels be with a high degree of probability considered typical of the condition of much if not all the analogous parts of the vascular system

The fundus oculi is the field available for ready examination of the small vessels If we consider the retina a prolongation of the brain through the optic nerve, changes in its circulation may with some reason be assumed to be also present in that of the rest of the encephalon It is the writer's opinion that any survey of the cardio-vascular system that does not include a thorough ophthalmoscopic examination may be misleading as it is incomplete Of as much importance as the discovery of the commoner retinal pathologic changes is the correlation of such changes with the other and more general findings In this the medical man has a great advantage over the specialist The practiced internist is quite capable of judging the character and extent of most retinal vascular changes

Vascular Spasm This is a debata-

ble condition but from close study of many fundi the writer is convinced that patients with early essential hypertension present frequent variation in calibre with a tendency to contraction of the retinal arteries and with this a varying degree of pressure upon the retinal veins at the crossing of vein and artery This has been noted particularly in a prolonged study of cases presenting the hypertensive type of the toxemia of pregnancy where hospitalization and close observation have been possible

It may be said that vascular spasm when present with a labile blood pressure serves as a suggestion or prophesy rather than as an established fact of peripheral vascular changes

Tortuosity of the Arteries This is of two kinds One may involve the larger vessels alone as wide, sweeping curves often without other evidences of vascular change This does not necessarily imply an arterio-sclerosis The other involves the smaller vessels along with the larger in curves of small radius so that the vessel is of a somewhat corkscrew form Such tortuosity almost always implies serious vascular change

Increased Light Reflex Widening of the central streak of light along the course of the artery especially when combined with a striking change in color to a silvery sheen or forming an almost white band, often of varying width, is of considerable import when associated with other changes

Variation in calibre and contour of individual arteries is often patent to the practiced eye and is of importance in prognosis This change seems particularly but by no means exclusively

a feature of cases with syphilitic background

Constriction and displacement of veins at the crossing of arteries is one of the easiest changes to detect and one of the most significant. This may vary from the slightest indentation such as may transiently mark the spastic cases to an apparent entire cutting off the venous stream and the sharp lateral and segmental displacement of the vein.

White patches may be of two kinds. One type is made up of small white flecks or wedged shaped minute spots rather diffusely scattered over both retinæ. These seem to be associated with comparatively benign types of hypertension. The other kind is characterized by a few large white areas at times reaching half the diameter of the optic disc. These are often attended by hemorrhages or marginal flecks of black pigment, evidence of former hemorrhage, and seem to attend the more serious examples of vascular disease.

Hemorrhages, whether small or large, when attended by definite sclerotic changes in the arteries are always serious and are one of the most valuable of prognostic signs. To be sure, one must differentiate the hemorrhages of inflammatory and toxic origin unattended by arteriosclerosis.

Thrombosis when attending serious vascular degeneration may be placed in this same category with hemorrhage.

The Central Nervous System. Evidence of vascular degeneration in this important field can be inferred from like changes in the retina and from certain results of impaired circulation. The latter are the probable conse-

quence of ischemia from vascular spasm or from thrombosis or hemorrhage. These may be transitory or permanent. They may vary from momentary vertigo or aphasia to passing or permanent mono- or hemi-plegia, or a vascular accident serious enough to result in death. Although minor attacks of cerebral ischemia may occur several years before death they are usually among the most ominous of the consequences of vascular disease. The changes in mentality characterizing arteriosclerosis are not to be passed over in considering prognosis.

The visceral circulation especially that of the kidney and pancreas may be sufficiently altered as to disturb the function of these important organs in a readily recognizable manner. In the presence of widespread cardiovascular disease the finding of a high specific gravity, marked albuminuria with numerous red blood cells and hyaline casts is good evidence of an arteriosclerotic kidney. Usually there is a moderate increase of uric acid in the blood in cases of this kind. Only in the later stages may there be retention of nitrogen. Such retention may be due to cardiac insufficiency, to superimposed inflammatory degeneration of the kidney or to coalescence of enough foci of anemic necrosis through arteriosclerosis to abolish the factor of safety in the kidney. Tests of renal function here as in other conditions are of no value until this factor of safety is abolished. It may be said in general that established signs of an arteriosclerotic kidney usually attend examples of advanced cardiovascular disease and, therefore, make for a grave prognosis. One fact needs emphasis,

cases of essential hypertension rarely die from uremia

It may be said that the mild diabetes of later life so often found with arteriosclerosis has for its basis arteriosclerotic changes in the vessels of the pancreas. O'Hare found such changes in a considerable percentage of examples of cardiovascular disease with hypertension. Glycosuria, since it usually attends advanced cases, is always a serious factor in prognosis and seems to have about the same weight as the manifestations of the arteriosclerotic kidney.

#### SUMMARY

The salient points in the prognosis of high blood pressure may be summarized. Unfavorable features are a family history of cardiovascular disorders, a relatively high diastolic pressure and, chiefly, evidence of degeneration in certain selected parts of the cardiovascular system. These evidences are of marked arteriosclerotic changes in the cerebral, retinal, coronary, renal or pancreatic arteries or in the aortic arch. Signs of myocardial weakness make for a bad prognosis. Among the functional tests, that re-

vealing a lack of normal response to effort on the part of pulse rate and blood pressure, when existing with advanced structural changes in the circulatory system, is a not unimportant item in an unfavorable prognosis. This is especially true where both systolic and diastolic pressures are fixed at high levels and do not vary after effort.

Of the favorable features the following may be mentioned. High blood pressure in the absence of demonstrable organic cardiovascular changes may not shorten life. This is especially true of cases in women appearing about the time of the menopause. High blood pressure with predominant changes in the larger peripheral vessels and with little change in the aorta or retinal vessels may be viewed with much less concern than those with marked changes in the smaller arteries. This is particularly true of cases with normal diastolic pressures and of those without albuminuria and glycosuria. Cases retaining their capacity to respond by a normal or exaggerated rise in blood pressure after effort carry a better prognosis than do those in which this capacity has been lost.

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# Arterial Hypertension\*

By GEORGE C HALE, *London, Ontario*

**A**RTERIAL hypertension, according to the dictionary, means abnormally high blood pressure. Now the original comprehension of the term, blood pressure, was the pressure of the blood upon the arterial wall such as would be recorded by a canula inserted into an artery and attached to a manometer. This is not practical from the clinical point of view, and as the possibility of error in the estimation of this pressure by the clinician's finger was great, the sphygmomanometer, or blood pressure apparatus with which we are all familiar, was introduced and has come to be a part of almost every physician's armamentarium.

However, with this apparatus there is liable to be considerable error for the following reasons—When we attach the armlet and inflate it sufficiently to obstruct the flow of blood so that there is no radial pulse, we are not only measuring the pressure of blood upon the arterial wall, but the pressure necessary to compress the wall itself sufficiently to obstruct the blood flow. In other words, a certain measurable pressure is required to compress the walls of an artery sufficiently to prevent the flow of a fluid

not even under pressure. Experiments with an artery removed from the body within two hours after death and before the vessel had lost that tonicity of wall which the living muscular coat gives it, have proved that a pressure as high as 100 mm mercury may be necessary to compress the wall sufficiently to prevent water flowing through by gravity.

An artery removed shortly after death of the patient will contract and thicken by mere handling and it is probable that the same phenomenon occurs when pressure is exerted during life by the armlet of the sphygmomanometer. This thickening of the wall and narrowing of the lumen would necessitate greater pressure to compress the vessel with consequent rise in the estimated systolic blood pressure. As the artery tired and relaxed the pressure would apparently fall. Here may be the explanation of the frequently observed fact that if the blood pressure is taken three times in succession, the third reading will be lower than the first. So when we measure systolic blood pressure clinically the factors with which we are concerned are not only peripheral arteriolar resistance, but the consistency of the wall and the internal calibre of the brachial artery.

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When the ventricle ceases to contract and passes into diastole, the blood pressure does not cease but there is a recoil by the artery wall which, as it were, passes the blood forward with a measurable pressure called the diastolic blood pressure. The second bulb in the sphygmograph, the bag of the bagpipes, and the compression chamber of the fire engine together with a nozzle in each instance provide a similar arrangement for maintaining a constant flow at a given pressure.

Normal systolic blood pressure is given variously in text-books as from 105 to 145 mm of mercury, normal diastolic pressure as from 20 to 50 mm lower, making the normal so-called pulse pressure 20 to 50 mm. Various conclusions have been set forth by writers regarding the significance of the pulse pressure, but it is a question whether these are justified in dealing with such a variable factor.

Without going further into the question of the accuracy of our methods of determination of actual blood pressure, or the importance of diastolic pressure and pulse pressure, let us consider the question of the significance of high blood pressure, or arterial hypertension.

For many years its presence in cases of nephritis or vascular disease was not considered strange, and was explained as resulting from a call on the part of nature for a rise of blood pressure to enable sufficient blood to be forced through the sclerosed kidneys or through arterioles of lessened calibre, just as more pressure is required to force water through rusty pipes of diminished lumen.

Only in comparatively recent years has arterial hypertension been unmasked and recognized, not as a disagreeable, but necessary result of nephritis and arterio-sclerosis, but in many cases a traitor guilty of actually causing these two diseases with which it is so frequently associated.

As a result of this unmasking, cases of arterial hypertension were studied from a new perspective, the wood was finally discovered in spite of the trees, and instances were reported of death from this disease without autopsy findings of nephritis or vascular pathology.

Let it be granted that arterio-sclerosis can cause arterial hypertension and that the latter may be due in some instances to renal arterio-sclerosis, to arterio-sclerosis of the medulla as suggested by Starling, or even to coronary sclerosis and so forth, there still remains a large group of cases which cannot be explained by such means and where the etiological factor remains obscure.

To this entity of idiopathic or essential hypertension the name of hyperpiesia was first applied by Sir Clifford Allbutt. His original definition reads as follows—"Hyperpiesia is a malady in which at or towards middle life, blood pressure rises excessively a malady having a course of its own, and deserving the name of a disease." He goes on to say—"Of hyperpiesia I have never offered an explanation or nothing more than conjecture. I have been content to distinguish it as a clinical series from recognized forms of Bright's Disease."

There are some who still hold to their former tenets that hyperpiesia is the result of precursory renal pathol-



ogy because it is so frequently accompanied or closely followed by evidence of disturbed renal function. The latter is to be expected, as is evidence of pathological changes elsewhere resulting from secondary arteriolar fibrosis, if the scientific eye were not focussed so persistently on the kidneys to the exclusion of other organs. Batty Shaw reports nineteen cases of hyperpiesia which died with clinical evidence of uremia. Of these there were three cases which showed no renal change whatever. He argues that uremia was impossible in these three cases, and by deduction improbable in the other sixteen. To properly evaluate this statement, however, one would have to be sure just what is meant by the term uremia, a question which suggests depths too deep to plumb in this short address.

The difficulty in studying the pathology of those dying of hyperpiesia lies in the fact that few actually die of this condition, but rather from the effects of continued hyperpiesia upon the arterial system. In cases dying early from some intercurrent disease while suffering from hyperpiesia, the picture is liable to be clouded by the effects of the intercurrent disease on the organs.

Much experimental work has been done in an attempt to discover the probable origin or identity of some pressor substance in the blood capable of producing the vasomotor excitability and resulting sustained arterial spasm which we call hyperpiesia.

Search has been made for some abnormal pressor substance produced by disturbed metabolism, or normal substance produced in undue amount, or

in normal amount but acting on a hypersensitive sympathetic nervous system.

In connection with faulty metabolism it is of interest to note the frequent relationship of obesity, diabetes, and gout to hypertension, and to recall the pressor effect of guanidin and creatinin, which may be produced in relatively large quantities by perverted metabolic action.

The endocrine system has been considered as a probable factor due to the occurrence of hypertension during the menopause and in hyperthyroidism, and also because of the well known effect of adrenalin on blood pressure. The suprarenal glands, however, are not enlarged in hypertension, and no one as yet has succeeded in demonstrating adrenalin in the blood in this disease.

Working on the theory of pressor substances being produced as the result of degeneration or disease of certain organs such as kidney, liver, spleen, etc., investigators have made extracts of these and injected them into animals and humans. The main effect in every instance, except that of kidney extract, has been a depressor and not a pressor one, i.e., the blood pressure was lowered. The fact that kidney extract can exert a pressor effect might explain the hypertension in some cases of chronic nephritis, but it does not offer a solution as to the cause in those cases where at autopsy the kidneys have been found normal.

Certain results are inevitable in continued hypertension. 1. The heart hypertrophies, as one would assume any muscle would do in response to a demand above the ordinary. If the my-

ocardium is healthy the heart may remain competent for many years or permanently unless peripheral resistance becomes too great, when the organ, sound though its muscle may be, finds itself unable to force blood against this enormous resistance, capillary stagnation supervenes, and the patient dies of cardiac defeat. If the myocardium is diseased the owner may succumb to an early cardiac death. 2 The arterioles undergo a sclerosis, due either to the inordinate strain to which they are subjected, or to an unknown toxin, or both. This means, as far as the organ or tissue supplied by the sclerosed vessels is concerned (a) less blood, (b) less gas and chemical exchange, (c) less detoxication, resulting in (d) accumulation of waste products, (e) less efficiency and coordination, (f) more fatigue, with the end result of atrophy and fibrosis of that organ.

The clinical picture will depend on which organs are chiefly affected by this arterio-sclerotic process, and the most characteristic pictures are those in which the greatest sufferers are the cerebral, coronary, or renal arterial systems, giving us the syndrome we characterize as apoplexy, angina pectoris, or azotemic nephritis.

It is of interest to note that, in spite of the agreement of the almost universal affection of the renal arterial system in hypertension, Romberg reckons that 45% of cases die of heart failure, 45% of apoplexy, and only 10% of uraemia.

There have been many attempts to classify hyperpiesia clinically without much success. Probably the most popular classification is that of benign and

malignant hypertension. Rowntree defines malignant hypertension as occurring in about 10% of all cases, of an unknown cause with a stormy and rapid progress, the diastolic blood pressure disproportionately high, neuroretinitis common, and cerebral renal and cardiac symptoms frequent, the prognosis grave, and treatment unsatisfactory. It would be impossible to classify hyperpiesia clinically from the height of the systolic blood pressure, as has been suggested, as cases of undoubted and previously proven hypertension may show normal blood pressure some months before death. In fact, pathologists usually assume that primary hypertension was present in life when at post mortem examination is found a high degree of left ventricular hypertrophy not associated with valvular disease, adherent pericardium, syphilitic aortitis, chronic glomerular nephritis, or hyperthyroidism.

Writers of an imaginative turn of mind have attempted to describe a human type as prone to develop hypertension. The disease, however, is too protean to allow of such easy characterization. We have all encountered it in the sallow, intense, and tired business man, in the choleric and ruddy squire with his foot bound up in a pillow, and in the pasty and lazy fat boy of Dickens now grown up.

Hypertension, like diabetes, is especially vicious in early life and relatively benign in the elderly. It is, however, the early cases, before the occurrence of arterio-sclerosis, which respond most favorably to treatment. With regard to elderly arterio-sclerotic cases who have had moderate hyper-

tension for many years without the occurrence of grave symptoms, adopt the attitude of Joslin regarding diabetes. Joslin says, "If a diabetic has known enough to live ten years, be sure you know enough to make him live another ten years before you tamper with him. The old diabetic has arteries so hard that his status must be changed as delicately as you would move a choice piece of bric-a-brac." The same rule applies to the elderly arteriosclerotic with high blood pressure. Many of them undoubtedly have an optimum blood pressure below which they cannot be forced without disaster.

The question of treatment of hypertension covers a very large field including as it must many associated or terminal conditions such as hypertension plus apoplexy, plus angina pectoris, plus uremia, etc.

Treatment on the whole is unsatisfactory. This is to a certain degree due to the following facts—(1) A large percentage of cases will show a temporary fall of blood pressure with

each new doctor consulted, or each new treatment tried. (2) Many of the remedial agents cause a purely temporary drop of blood pressure at the time of their exhibition. (3) In many instances, if one succeeds in lowering the blood pressure, the patient feels much worse.

If there is some readily ascertainable and removable cause such as focal infection, intestinal intoxication, obesity, abuse of alcohol or tobacco, or a misconception on the part of the patient as to the amount of work and worry that is his share in this world, there may be some cause for optimism on the part of the physician. If, however, the removal of such causes does not lead to improvement, the results will be disappointing.

Time and space do not permit one to go into detail regarding the present status of such therapeutic agents as therapy, etc. Each has its optimists, liver extract, the sulphocyanates, veratrum viride, diathermy, hydro- its pessimists, and its merely hopefuls!

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# Radiation Therapy in Malignant Disease—Results To Be Expected\*

By GEORGE E. PRAHLER, M.D., *Professor of Radiology in the Graduate School of Medicine of the University of Pennsylvania, and Chairman of the Committee on Cancer Control of the Philadelphia County Medical Society, Philadelphia*

WITH our present knowledge of the treatment of cancer, good results can only be obtained by the early recognition of the disease and by the immediate, thorough and skillful treatment. The fear of operation on the part of the patient is an important factor in causing delay. If this fear can be eliminated by the family physicians and the consultants, who know that radiation is of definite value in the treatment of malignant disease, patients will be more likely to consult the family physician at once, instead of going to quacks, or doing nothing. Postponement is most often due to fear of operation, or failure to realize the seriousness of the disease, and also due to the *absence of pain in the early stages*. It has seemed to us, therefore that a review of the results that have been obtained or that may be expected under given conditions should be of value to you as consulting internists. In this study, we must take into account our limitations as radiologists as well as our possibilities.

## SKIN CANCERS

*Practically all or approximately 100% of cancers of the skin can be cured by means of radium, x-rays, or electro-coagulation or by a combination of these methods, providing they are treated skillfully while they are still only cancers of the skin. When, however, the ordinary basal cell cancer of the skin (which can certainly be cured at the beginning) has invaded the deeper tissues, such as the cartilage or the mucous membrane of the nose, or fascia, muscle or bone, it then becomes a very difficult matter and requires the greatest skill and ingenuity.*

It is supposed by some that practically all skin cancers are of the basal cell type and that they do not give rise to metastasis. This is a mistake. Most cancers that develop on the hands or in scar tissue, and those developing in the temporal and zygomatic regions are very apt to be of the squamous cell type and they give rise to metastasis. Therefore delays, or inefficient treatment at the beginning of cancer is dangerous. The pigmented mole that has undergone malignant degeneration is the most dangerous of all and should be destroyed by electro-

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*coagulation* completely at one sitting, at the very beginning. There is sufficient means now available to remove moles easily, and satisfactorily, and it would seem advisable to have all moles removed for cosmetic reasons as well as for future safety, on the same basis that one carries fire insurance—even though probably not more than one in a thousand becomes malignant. Radium, x-ray treatment, or excision caustics are not satisfactory in the treatment of pigmented moles.

*Epitheliomata about the eyelids* are best treated by radium, or next best by the x-rays. Electro-coagulation is apt to lead to ectropion and is therefore less satisfactory. Excision often fails to eliminate all of the disease, probably due to the necessary attempt to conserve tissue.

#### EPITHELIOMA OF THE LIP

In 82 primary cancers of the lip, without palpable lymph nodes, which were treated by electro-coagulation, by us, combined with high voltage radiation over the glandular area, 97.5% were cured. This illustrates the importance of thorough treatment at the beginning.

When the lymphatics are definitely involved, the only hope from radiation treatment is by the use of highly filtered gamma radiation, and sometimes combined with operation. *The results by means of any form of treatment or any combination will be less and less satisfactory, the more the disease has extended.*

#### CANCER OF THE MOUTH

The results from the most skillful radiation treatment of cancer of the

mouth vary so much with the stage of the disease and its location that it is difficult to make an accurate estimate briefly. The general average of all cases applying for treatment in all stages at which they now come under skillful treatment is about 25% of cures.<sup>1</sup> If these same patients can receive skillful radiation treatment *when they first come under the care of a physician*, at least 50% should be cured, and *if patients can be educated to apply for this treatment when lesions in the mouth first appear*, at least 75% should be cured. In a review of the work done at the Radiumhemmet, at Stockholm, Forsell,<sup>1</sup> found 62, 62, and 56 per cent after one, three, and five years respectively, in primary operable tumors. In cases with regional metastasis he advises operation combined with radiation, and by this combination obtained cures in 35%. Haggstrom's<sup>2</sup> surgical statistics, the figures of which do not fall below those of other statistics published on the same subject, show 31% of healings with lasting effect for five years (20 cases out of 64). The corresponding figure for exclusively radiological treatment of operable primary tumors is 56% (16 cases out of 29), and for the combined surgical and radiological treatment 60% (13 of 22). It is clearly evident therefore that radiation alone, or radiation combined with surgery is the best form of treatment in cancer of the mouth in the operable stage. Forsell, makes the following observations:

"1—With radiological healing the percentage of *recurrences* is very low when once complete freedom from

clinical symptoms has been obtained and has been maintained for one year

2—With the technique employed, and with the clientele represented, a permanent healing was only obtained in those cases in which the disease was still macroscopically confined to its primary site. In none of the 72 cases in which there was unmistakable regional metastasis to the lymph nodes, was healing obtained for as much as one year" (In all these cases, the glandular metastases were very extensive, they were inoperable, and in poor general health)

In 68 primary, *operable and inoperable cases*, without palpable lymph nodes, there were 31% five year cures, in Forsell's records, Buchanan,<sup>3</sup> gives 20 months as the natural duration of cancer of the tongue

*My records as reviewed by Dr B P Widmann show Primary Carcinoma of the tongue with no lymph nodes, 55% were well from 4 to 15 years Primary Carcinoma of the Tongue, with lymph nodes, 40% are clinically well from 1 to 5 years Unless the glandular involvement is very extensive, we think the chances of recovery are fairly good Counting all the tongue cases, of all grades, 23.6% are apparently cured In our group of 78 carcinomas involving the inside of the cheek, 15 were too far advanced for any kind of treatment, leaving 63 cases for classification Among these 63 cases the alveolar process was involved in 28 cases Of 20 primary cases, with no glands, 13 or 65% recovered Of these 13 that recovered, two died of intercurrent disease and the other 11 cases or 55% are well from 1 to 15 years Carcinoma of the cheek with*

*glands showed 11% well 3 and 5 years It seems to me that from 50% to 75% of all cancers of the inside of the cheek as they first come to the physician should be cured, if treated thoroughly and skillfully at once by gamma radiation*

#### CANCER OF THE TONSIL

Cancer of the tonsil is infrequent as compared with other malignant lesions about the mouth Matthews<sup>4</sup> concludes that practically all cases are *urgically inoperable* The prompt recurrences following surgery in the apparently localized lesions, indicates that there is usually widespread infiltration at the base With tonsillectomy alone, in 20 cases of sarcoma and 3 of carcinoma, not one was reported to have lived 2 years without recurrences On the other hand, *malignant* disease of the tonsil seems to be rather sensitive to radiation Schirmer,<sup>5</sup> reports 15 cases with no gland involvement and of these one case was clinically well after radiation Forsell,<sup>6</sup> reports on 31 cases with 9% clinically cured Quick,<sup>7</sup> reports on 124 cases of carcinoma of the tonsil, with 22.5% clinically cured by radiotherapy for an average duration of 26 months

#### OUR STATISTICS

In our group of 24 cases of carcinoma of the tonsil, 3 cases were too far advanced for any kind of treatment Of 3 primary cases without palpable lymph nodes all are clinically well 1½, 3, and 4 years, treated by the *saturation method* of roentgentherapy Of 8 primary cases with metastasis, one is well 7 years, one which was clinically well died of intercurrent dis-

ease All of the recurrent cases died of the disease

It would seem advisable to treat all malignant disease of the tonsils by gamma radiation, or if not recognized until after operation to give immediate post-operative treatment, locally and externally by gamma radiation

CARCINOMA OF THE BREAST

Cancer of the breast is a surface growth which should be recognized in its earliest stage If removed surgically while it is strictly confined to the breast, theoretically there should be 100% cures Practical experience however, shows that only about one out of five reach the surgeon in this early stage, and that as a matter of fact

even in this supposed early stage only about 70% are cured.

Four-fifths of the patients reach the surgeon only after the disease has extended at least to the lymph nodes in the axilla and of these surgery shows approximately 22% cures, when radiation is not added. *When radiation is added to operation we may expect approximately 46% cures*, or about twice as many cures as from operation alone In a review of 1066 privately treated cases of carcinoma of the breast we,<sup>8</sup> found 68% of the early operable cases living at the end of 5 years and of the late operable with gland involvement 46% were alive at the end of 5 years when radiation and operation was used

Comparative Values of Other Clinics and Methods (Operable Cases)

			Alive 3 years		Alive 5 years	
			No Glands	With Glands	No Glands	With Glands
			Percent	Percent	Percent	Percent
Greenough		Surgery	47	19		
Konig		"			100	39
Bloodgood	.	"			70	20
Lee	.	"				15
Finsterer	.	"				43
Doederlein	.	"			46	5
Doederlein		" and radiation not completed			48	20
Doederlein	.	" and radiation totally completed			80	48 36
Wintz		" and radiation both groups 77%			61	42
Schmitz	.	" and radiation			68	46
Pfahler & Widmann						

Upon theoretical grounds, I have been recommending pre-operative treatment during the past 12 years, and post-operative treatment during 25 years<sup>9</sup> Now some brilliant experimental work has been done by Murphy,<sup>10</sup> and his associates at the Rockefeller Institute, and by Russ and Scott,<sup>11</sup> in London in which experiments they exposed only small areas

of tissue with 50, 65, and 100% of an erythema dose, leaving a central area unexposed They then innoculated Jensen's rat sarcoma into this central area and in all instances the tumor grew in the unexposed tissue leaving to a great extent the areas treated in advance by x-rays uninvolved To me these experiments are very convincing, as to the value of pre-operative treat-

ment Clinical proof is shown by our own experience, and also by Forsell, at the Radiumhemmet in Stockholm, in which he gave pre-operative treatment to 169 cases and 51.5% were free from symptoms from 1 to 7 years. It seems therefore, to be definitely shown that radiation combined with operation may be expected to double the cures obtained by operation alone; that radiation will give much palliation in inoperable cases, and that some inoperable cases can be made operable.

#### CARCINOMA OF THE UTERUS

Cancer of the uterus like cancer elsewhere in the body is best treated in its early stages, or better treated by eliminating precancerous conditions. *If all lacerations are properly and promptly repaired, all cervicitis thoroughly treated and any vaginal discharge investigated at once, many cancers will be prevented.* If to this a thorough periodic health examination is made biannually of women, especially after 35 years most cancers of the uterus will be recognized in an early stage, when we may expect from 50 to 80% of cures by thorough radiation. In fact, in the report by Seuffert,<sup>12</sup> from the Doederlein clinic in Munich, it was found that the operable cases who had followed through the complete treatment, 80% were well at the end of 5 years. This then is the best chance for the woman who comes early and has thorough and complete radiation treatment. When one studies the general average of all patients who come to a clinic for treatment, the results are not nearly so good.

In the report of the Ministry of Health in London, published 1927, Dr Lane-Clayton in comparing statistics of 6,661 cases operated on either by vaginal or abdominal hysterectomy, 2,272 were alive at the end of five years, making 34.1%. In the case of 1,117 "Operable" cases treated only by radiation, 400 were alive at the end of five years, which equals 35.8%. The end results, therefore, in a large series of operable cases are about the same, but with operation there is an operative mortality of 17 per cent.

Of all cases who presented themselves for treatment, operable and inoperable, 18.3% were alive at the end of 5 years, while radiation of a similar group gave 22% of 5 year results.

Ward and Farrar,<sup>13</sup> studied a total of 134 cases treated by radiation from 1919 to 1923 and at the end of 5 years 23.1% are living. Of the 32 operable and borderline cases in this series, 53.1% are living.

The earlier, the more thoroughly, and the more skillfully cancer of the uterus is treated, the better will be the results no matter whether it be by operation, or radiation. There is no other practical method known. The choice as to operation or radiation in any particular case will depend somewhat upon the skill and facilities available, but this choice can only be applied to the operable cases. In the surgical clinics the operable cases are 57% and in the radiological clinics the operability is 29%, leaving 33% and 71% respectively that can only have a choice between radiation or nothing. From a study by Heymann,<sup>14</sup> of 19 operative clinics, the operability rate



was found to vary from 81 to 157% or an average of approximately 57% while in 13 radiological clinics, the operable cases varied from 51 to 153% or an average of approximately 29%. It will be seen therefore that a very much more favorable group of cases is seen in surgical clinics. It is likely that in considering surgery the family physician decides in many cases that the patient is inoperable and does not send the patient to the *surgical clinic*, while all classes are sent to the *radiological clinic*. This is a compliment to radiotherapy, but tends to lower the total statistical values.

Even in those gynecological clinics, (Baisch, Doederlein, Menge, Kehrer, Wintz) in which surgery was abandoned for radiotherapy and in which the same methods of classification were utilized, the percentage of operable cases was very much lower and a more hopeless class of patients applied for treatment when it became known that only radiological methods were used. In Doederlein's clinic, for example, 265 cases of cancer of the cervix applied for treatment during the 5 years including 1908 and 1912, of which 63.02 percent were operable, while surgery was used, and in the years of 1913, 1916, when radiation was adopted, 500 cases applied of which only 33.9% were operable—about one-half as many were operable but about twice as many patients applied for treatment in a similar period. The fear of operation causes much delay and when it is known that the earliest cases have even a better chance with radiation therapy, patients will apply for treatment earlier. For example, at the Radiumhemmet in Stockholm,

the operability rate has risen from 29.1% in 1921 to 59.2% in 1925.

From a study of the statistics from 20 of the leading gynecologic clinics of the world in which *surgery* was used, and in which 5,805 patients applied for treatment, there were 19.1% of five year cures. This percentage drops to 18.7%, if the study is confined to the eleven largest clinics in each of which there is recorded at least 200 applicants.

From a study of the statistics from 17 radiological clinics and counting all applicants 3,512 there was obtained 16.3% five year cures. In comparing the results of 19.1% from surgery, with 16.3% from radiation therapy it must be remembered that *the radiological material only contains about one-half as many operable cases*.

The primary mortality in 3,257 cases of cancer of the cervix operated upon in 24 leading clinics was 17.2%. The primary mortality for radiological treatment is usually considered negative, but Heyman, in reviewing the 502 cases treated at the Radiumhemmet found 8 patients or 1.59% who died in immediate connection with the radium treatment.

If one confined the statistics to the operable and borderline cases only it is found from a review of 24 of the leading surgical clinics in which 3,659 cases were operated upon, there is a five year recovery of 35.5% while 12 radiological clinics gave a general average of 34.9%. In the radiological treatment of 145 cases at the Radiumhemmet in Stockholm, there were 5 year cures of 46.2%.

In dealing with the operable cases, with radiological treatment, it must

be borne in mind that the treatment involves relatively little inconvenience, as compared with an extended operation and that while 54% are not well at the end of five years, the majority of these 54% of patients have palliative relief, and may be free from symptoms for one or more years, and that the immediate mortality is eleven times as great from operations as from radiation

Only a few statistics give a statistical account of the morbidity either from operation or radiation Davis,<sup>15</sup> reports 17 cases of primarily healed abdominally operated cases with the development of urinary fistulae in four cases (25%) and another four cases developed pyelitis, thrombosis, cystitis and suppuration respectively, and Gaydoul and Schmidt,<sup>16</sup> report from Hofmeier's clinic five cases of damage to the urinary tract among 50 abdominal operations Among 502 cases treated radiologically at the Radiumhemmet from 1914-1921, 54 cases, 15% gave some rectal reaction (tenesmus, pain, bleeding from the bowel, impaired general condition, fever) with ulceration in 13 cases, and the fistulae only (1%) result in permanent inconvenience The deaths (159%) occurred in the septic cases from peritonitis

The palliative results obtained by Heyman, in 375 patients which were not well at the end of 5 years and which are counted a failure obtained relief from hemorrhage in 90% with 23.4% remaining free after 2 years Pain was relieved in 53% and 28% remained free at the end of 2 years Of 231 cases unable to work at the beginning, 61.6% were returned to

work and 30.3% remained at work at the end of 2 years

It will be seen therefore, that all in all, radiological treatment when applied skillfully gives the better results in any stage of cancer of the cervix

### CANCER OF THE UTERINE BODY

In most statistics cancer of the body makes up about 10% of the total cases of cancer of the uterus In nine surgical statistics, studied by Heymann, the operability percentage varied from 62 to 100% and the five year cures varied from 24.0 to 59.1% or an average of all applicants (318) of 42.8 percent, and 58.8% of only operable cases are counted Of the total number of cases (46) treated by radiation at the Radiumhemmet from 1913 to 1921, 45.7% were well after 5 years, while if only the operable cases (25) are considered 60% were well after 5 years, when treated by radiation Therefore, it will be seen that the end results from skillful operation or skillful radiation is approximately the same

Time will not permit the discussion of cancer in all parts of the body The subjects which I have discussed cover the fields in which radiation has been shown to be of superior value In my opinion, however, we may summarize the subject as follows

1—Cancer of the *skin* can be cured by electro-coagulation and radiation in practically 100%, if treated early

2—Cancer of the *mouth* should be cured in from 50 to 75% of cases in the early stage

3—In cancer of the *breast* 45 to 75%

should be cured with operation combined with radiation, if treated early, depending upon the extent of the disease

4—Cancer of the uterus should be cured by radiation in from 45 to 75% if treated thoroughly and skillfully in the earliest stages

5—Cancer anywhere in the body can generally be retarded by radiation, but in visceral carcinoma, operation should not be delayed for radiation, but on the other hand all operations for cancer should be followed by radiation, either with radium or x-rays depending upon the condition

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# Can or Will the Internist Practice Preventive Medicine?\*

By GEORGE H. BIGELOW, *Boston, Mass.*

**I**N the presence of the clinician the health officer is apt to feel a self-conscious gratitude, "gratitude" because of the satisfaction that comes from mingling with those in the more established and time honored branches of the profession; "self-conscious" because many of the profound social, economic and medical readjustments with which the doctor is faced are blamed on the health officer and his ilk. But it is important that such mingling should not only be allowed but encouraged, in order that each may understand the profound difference of their points of view. The doctor must use every resource to protect the individual from his environment, while the health officer must in his turn strain hard to protect the environment from the individual. It is the same telescope but they are looking through it from different ends. But the world is full of profound differences in points of view. the lawyer and the judge, the autoist and the traffic officer, the commercial drug house and the pharmacologist, the mortician and the clinician; the cosmetist and Mr. Zeigfield, the bootlegger and the prohibitionist. Just think of the benefits

that would come from an address by each of these conflicting groups to the other. Antithesis might become synthesis. Yet perhaps that might in the end be undesirable!

Let me illustrate the divergence in point of view of the practitioner and the health officer from our recent experience. We are profoundly interested in identifying and controlling the typhoid carrier. A member of a family in which there is a case gives a history suggesting typhoid fever twenty years ago. Yet the doctor is unwilling that we should examine specimens because he has "known her for five years." Physicians advise against typhoid prophylaxis of other members of the family, although half our typhoid is secondary. Dr. X agrees to report his communicable disease provided Dr. Y will do the same. Each waits for the other to start. Toxin-antitoxin is ridiculously little used in private practice though diphtheria still kills more children than automobiles. An occasional doctor talks of "state medicine" when the health officer strives for adequate examination of the children in the family of a tuberculous. Yet only 20 per cent of the tuberculosis in Massachusetts is reported in a favorable stage of the disease! In venereal disease control the con-

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flict in point of view is often the most readily apparent. One of the principal causes of white hair among health officers is the practitioner who varies his advice as to length of quarantine as he goes along. "There is the law", you say. But how futile is the law in the presence of so-called "misunderstandings"

Some resent cancer education which brings three or more persons to a physician without cancer for every one with it. Hysteria, they cry. Nonsense! It is not fact but fiction on which hysteria is based. Then there is the whole brawl of divergent opinion in regard to tonsillectomy, the importance of care of the deciduous teeth, and a hundred and one other matters. There are even physicians who advise against pasteurized milk! I sometimes think that certain members of the medical profession have delayed increasing the safety of our milk supply more than any other group.

I have, of course, selected instances ruthlessly to over-emphasize my point. On the other hand, I could give examples of the practitioner with a profound sense of community responsibility, who has made his peace with Hippocrates and his oath, and who deserves to be known as a health officer in his community far more than the individual who may strut fatuously under the title, devoting his life to fumigation, tin cans and ashes. But that is the other side of the shield.

We must get to the question of "Can or will the internist practice preventive medicine?" To answer this we must have definitions. What is an internist? I have nothing profound to

contribute here. But it would seem to me that the internist, while making use of all the advances and complexities of medical knowledge, is the direct descendant of what suffering mankind so cherished and has now largely lost, the family physician at his best. He individualizes his advice not to the organ involved but to the whole patient, mental and physical, and to his family and his whole environment. To do that wisely in all instances would make Solomon hang his head!

What, on the other hand, is the practice of preventive medicine? Some lay people confuse it with birth control. We know the diseases against which we have effective prophylaxes, and others will be added unto them. We know how some diseases are spread and should not keep it as the secret of the Sphinx. We know something of the conditions that menace the pregnant woman, the infant, child, youth and adult, such as foci of infection, extreme deviation in weight, preposterous hygienic habits, and improper bodily mechanics. There is, of course, much more that we do not know. What are the extremes of the physiological normal in blood pressure, temperature, albuminuria, serology, diet, and the like? How far from normal must the person be in order to warrant his visiting a doctor without a suspicion of hysteria? The dentists say he should come regularly irrespective of pathology. The enthusiasts for health examinations say the same.

But for the effective health examination we must have a public which knows how to use such an examination. A despairing physician told me of an enraged woman whom he had

examined healthily. On vague suspicions in the chest he called for an X-ray. With delight he informed her that it was negative. In no uncertain terms she told him of her opinion of him for putting her to the unnecessary expense. She was in the dark ages when it was considered an admission of weakness if a doctor was ever seen reading a medical book. The doctor on his side was through with health examinations until the public was educated as to what to expect. Again, an enraged man said that all he got out of his examination was advice as to tonsillectomy. When asked if that wasn't good advice, he said he supposed so but that he didn't need to pay for it again as three other doctors had told him the same thing. Of course, such people are lazy. They look for the miracle, the self-reducing soap. They expect from the health examination the effortless road to eternal youth. No fee is too high for the physician to charge who must suffer with them. They need mental dynamite.

But even for the intelligent public

do we know enough about these things at present to keep the sincere doctor on the one hand from being a backslapper and on the other from being a crepe hanger? Won't we lose more than we gain by rushing in without complete knowledge? Is not ignorance the basic reason why the magnificent potential inherent in examinations of the supposedly well has been so little realized? In large part. But if ignorance forbade medical practice, how many physicians would handle pneumonia, arthritis, undulant fever, the common cold, in fact, any condition to which flesh is heir. Such a philosophy would prohibit efforts to save 30 per cent of the cancerous, to still further reduce tuberculosis from its place as the most killing disease in the ages fifteen to thirty-nine, to save mothers and babies throughout the country. Ignorance is no valid excuse for not using what we know. The temper of the public and the dignity and responsibility of the profession demand that the internist practice preventive medicine as we know it. He can, but in how many instances will he?

# A Statistical Study Of The Coincidence Of Malignancy And Tuberculosis

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THE existence of a correlation, positive or negative, between any two major diseases is a subject which intrigues the mind of physician, statistician, biologist and layman. Two such fatal diseases as tuberculosis and malignancy have offered for many years a natural field for research and for speculation, and the literature abounds with case reports, statistical analyses and opinions as to the balance which the writer thinks to exist between these two conditions. A recent (and in fact the first thorough and statistically adequate) study of a large body of carefully prepared material is that of Pearl,<sup>1</sup> who concludes that "there is a definite and marked incompatibility or antagonism between the two diseases, cancer and tuberculosis, of such a sort that both occur together at the same time in florid activity in the same individual only with great rarity." It is the purpose of this paper to consider statistically the autopsy material from the Department of Pathology of the University of Michigan, and to analyze these statistics with a view to ascertaining any possible interrelationship of malignancy and tuberculosis. The statistical method has been essentially

that of Pearl, but the conclusions drawn from the analysis do not support his statement quoted above.

No attempt will be made to review the history of this problem previous to Pearl's study. This phase of the subject is thoroughly discussed by him and a very complete bibliography will be found attached to his paper (*loc cit*). Most of the writers have taken as a starting point Rokitsky's<sup>2</sup> dictum, based not on statistical information but rather on his own experience, that cancer and tuberculosis very seldom occur together either in the same organ or the same individual. They have then, on the basis of their experience, set out to disagree with or substitute this doctrine. The statistical analyses previous to Pearl's are not fully adequate, either from the point of view of the material or of the manner of treatment. The literature since this time consists of clinical case reports of combined tuberculosis and carcinoma by Ainto,<sup>3</sup> Klink,<sup>4</sup> Callahan, Schiltz and Hellwig,<sup>5</sup> and Graham.<sup>6</sup> In addition to these case reports there has appeared an experimental study by Cherry<sup>7</sup> and a statistical review by Carlson and Bell.<sup>8</sup> Further reference will be made to these two papers

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As already indicated, investigation of this problem has proceeded along three lines,—case reports, experimental investigations and statistical studies. Evidence based on the close association or lack of association of tuberculosis and malignancy in the same organ, while interesting, is contradictory and unconvincing. It has been held that certain organs, such as the ileum, where tuberculosis is common, relatively rarely show cancer, and on the other hand in the stomach, where cancer is often localized, tuberculosis is rare. Over against this observation are the numerous reports in the literature describing the close association of cancer and active tuberculosis in the same organ. It is impossible to draw any definite conclusions from such evidence.

Experimental work has followed two courses,—animal experimentation and the use of tuberculin in treating advanced cases of malignancy. As mentioned by Carlson and Bell (*loc cit*), the work on animals has not given uniform results. In 1926 Centanni and Rezze<sup>9</sup> injected mice (a type resistant to tuberculosis) with a transplantable adenocarcinoma. They found that live tubercle bacilli prevented tumor growth, tuberculin retarded it and dead tubercle bacilli had very little effect. Injecting tubercle bacilli directly into a tumor already present caused partial destruction, a result which can be produced also by injection of other toxic substances. When tumor and tubercle bacilli were injected in different parts of the body, the tumor growth was at first inhibited and then as the tumor developed

the tuberculosis regressed. When neoplasm was injected into an animal previously infected with tuberculosis, the neoplasm grew more slowly. They attributed their results to an allergic reaction against neoplasm, caused by the tubercle bacilli.

Cherry<sup>7</sup> in 1929 studied spontaneous neoplasms occurring in a tuberculosis-resistant strain of mice. He inoculated these mice with living tubercle bacilli and found that neoplasms occurred spontaneously much more commonly in the inoculated mice than in those not inoculated. He states that he recovered acid-fast bacilli from 10% of his inoculated mice, but he does not state how many of these mice showed tumors. Three tuberculomas occurred, and in the protocols of these mice no mention is made of any neoplasms. It is not clear just how many of the mice of the inoculated series, which showed the high incidence of neoplasm, actually had an active tuberculosis.

The published reports on the use of tuberculin in the treatment of cancer have come from the Johns Hopkins Institute for Biological Research. Only cases which were hopeless from a surgical standpoint were considered as suitable material, and hence the field was scarcely favorable for good results. The last publication, a preliminary progress report by Pearl, Sutton and Howard,<sup>10</sup> gives six case histories. Four of these showed definite clinical improvement at the time of the report, one had died, and the other one showed serious symptoms from brain metastases. This does not necessarily have any bearing on the relationship of active tuberculosis to

cancer. In the use of tuberculin, one is dealing with a toxic substance which happens to be a bouillon filtrate of a culture of tubercle bacilli. Even though tuberculin should be found a valuable instrument in fighting cancer, it is not proven that the disease tuberculosis inhibits malignancy.

In preparing the statistical material for this paper, the entire series of autopsy protocols of the Department of Pathology of the University of Michigan was studied. All cases in which a complete examination of the trunk had not been allowed, cases in which microscopic examination was not complete, and those in which the age, sex and race were not recorded, were eliminated. From those remaining, there were isolated the cases of malignancy. Each of these cases was then controlled by the next case, not a malignancy, following it in the autopsy series, falling within five years of the age, of the same sex and of the same race (white or colored). This treatment is essentially that used by Pearl in his analysis, *q v*. The only exception to this procedure was at the end of the series where those cases which could not be controlled by one later in the series, were controlled by the nearest one preceding which met the above conditions and which had not been already used. In this way cases in the cancer and control series are made comparable in time, thus eliminating errors arising from changing criteria or changing disease incidence, the possible error from the fact that malignancy is a disease primarily of later life than tuberculosis is eliminated, and sex and racial differences are equalized. A

total of 514 cases of malignancy was used and 514 controls were set up in this manner.

In considering the coincidence of tuberculosis in both the cancer and control series a distinction is drawn between active and healed tuberculosis. The simple presence of caseation is not taken as evidence of activity, because it seems that a well encapsulated area of caseation is no more active than an area of calcification. A lesion is not considered active unless tuberculous granulation tissue has been found microscopically and there was evidence of proliferation or spread of the disease process.

It is frankly recognized that in the diagnosis of healed tuberculosis much depends on the criteria used and the thoroughness with which the prosecutor searched for evidence of the disease. However, since the control and malignancy cases are comparable in time, and since all cases used come from the autopsy service of one man, Dr. A. S. Warthin, these variables should equalize each other in the two series. The only evidence accepted as indicating healed tuberculosis is the finding of healed tubercles, such criteria as apical scarring and apical adhesions being discarded as not uniformly diagnostic of tuberculosis.

The cases which were selected in this manner were tabulated, noting in each instance the major condition which was responsible for the individual's death. A summary of the results obtained is given in Table 1.

The results were further analyzed as to sex with the results given in table 2. Less than 1% of the cases in the total series are of the colored

race, so that this factor was discarded in analyzing the statistics

TABLE I

Malignancy Series—514 cases		
Active tuberculosis	27 cases	5.3%
Healed tuberculosis	126 cases	24.5%
Control Series—514 cases		
Active tuberculosis	58 cases	11.3%
Healed tuberculosis	150 cases	29.2%

TABLE 2

Malignancy Series		
Males		
Active tuberculosis	20 cases	5.4%
Healed tuberculosis	87 cases	23.7%
Females		
Active tuberculosis	7 cases	4.8%
Healed tuberculosis	39 cases	26.5%
Control Series		
Males		
Active tuberculosis	47 cases	12.8%
Healed tuberculosis	114 cases	31.1%
Females		
Active tuberculosis	11 cases	7.5%
Healed tuberculosis	36 cases	24.5%

It will be seen that while there is very little difference in the incidence of healed tuberculosis between the malignancy and control groups, the active tuberculosis, both in the total series and in the segregation by sexes, is practically twice as great in the non-cancerous group as in those showing some form of malignancy. These results are in close agreement with those found by Pearl and also by Carlson and Bell (*loc. cit.*) In Pearl's total series active tuberculosis was found in 6.6% of the malignant cases and 16.3% of the non-malignant cases. Healed tuberculosis occurred in 28.1% of the cancerous cases and 26.7% of the control cases. Carlson and Bell found also an equal incidence of healed tuberculosis in the two series,

but active tuberculosis was much more common in the non-cancerous controls than in those showing some form of malignancy. The method used by Carlson and Bell differs from that used by Pearl and in this paper. They do not consider the sexes separately, and they have charted their cases by decades, taking the percentage of tuberculosis in all post mortems, and in cancer cases falling in that age span. The close parallelism between the three series, taken from different sections of the country and using two such different statistical methods lends weight to the results obtained. It may be safely said that active tuberculosis is much more common in non-cancerous individuals than in those with some form of malignancy, while healed tuberculosis occurs in about equal frequency in both groups, if the comparison is made using as controls those who die from all causes except malignancy,—including among these diseases tuberculosis itself.

As already pointed out by Carlson and Bell<sup>8</sup> there is an important objection to the use of a group as controls in which all manner of diseases were fundamental in causing death. They have demonstrated that a similar apparent antagonism can be demonstrated between heart disease and malignancy, and between heart disease and tuberculosis. In my series of 514 cancer cases, practically all died as a direct result of the malignant condition, and in only 3 instances was death due to tuberculosis. In the control group, on the other hand, 34 of the cases of active tuberculosis died as a result of

their tuberculosis. The question arises as to how many of these cases might have developed cancer had they not died first of tuberculosis. Since the cancer and control series obtained are not entirely comparable, it therefore seems that the results which are tabulated above are misleading.

It does not, however, seem impossible to set up a series of malignancy and control cases which are more nearly comparable. In 24 of the 27, or 88.9% of the cases of active tuberculosis found associated with cancer, the tuberculosis was a secondary factor and not the condition leading to the individual's death. In setting up the new series for comparison the three cases dying of tuberculosis were excluded leaving a total of 511 cases of malignant disease. Similarly the 34 cases from the control series in which the individual died of tuberculosis were excluded. These vacancies were filled in by taking the next following protocol in the autopsy series, not already used as a control, which met the conditions already outlined for selecting controls (qv). This gives two series in which active tuberculosis, if present is not the primary, underlying cause of death. It was found that in the new controls taken three cases of active tuberculosis occurred with death due to some other factor, and these, of course, are added to the total cases of active tuberculosis in the control series. A summary of this new comparison is given in table 3.

It is evident that there is no significant variation in the percentage results in the cancer and control series as given above. The position is taken that these results more nearly repre-

TABLE 3

Malignancy Series	511 cases	
Active tuberculosis	24 cases	4.7%
Control Series	511 cases	
Active tuberculosis	27 cases	5.3%
DISTRIBUTION AS TO SEXES		
Malignancy Series		
Males	366 cases	
Active tuberculosis	19 cases	5.2%
Females	145 cases	
Active tuberculosis	5 cases	3.4%
Control Series		
Males	366 cases	
Active tuberculosis	21 cases	5.7%
Females	145 cases	
Active tuberculosis	6 cases	4.1%

sent an answer to the problem of whether tuberculosis and cancer are associated more often, or less often than tuberculosis and any other disease capable of causing death. In the series summarized in tables 1 and 2 tuberculosis combined with cancer was being compared with tuberculosis, —sometimes combined with some other major disease and sometimes the only serious condition from which the individual was suffering. Such a comparison is obviously apt to lead into error. In the series summarized in table 3, on the other hand, the tuberculosis is in every instance, in both cancer and control series, combined with another serious condition, and in fact with another disease which caused the death. This gives a cancer series and a control series which are comparable, and from a study of which it is impossible to demonstrate any correlation, positive or negative, between active tuberculosis and cancer.

The evidence from case reports, experimental work and statistics fails to establish any convincing relationship between these two diseases. The

fact that healed tuberculosis is found with equal frequency in cancerous and non-cancerous individuals shows that a past infection is without bearing on the development of malignancy. The position that the person with active tuberculosis is less apt to have a malignancy, because of an immunity to cancer, can not be substantiated by the statistics presented in this paper. He is less apt to have cancer because he may die of his tuberculosis before he reaches the age at which cancer is most common. The occurrence together of the two diseases appears to follow closely the occurrence of tuberculosis with other serious diseases capable of causing death.

#### SUMMARY

1 Investigation of the concomitant occurrence of cancer and tuberculosis by means of case studies yields many interesting reports but no valid evidence of the frequency of the combined diseases.

2. The results from animal experimentation are contradictory and inconclusive.

3 The result obtained, or the lack thereof, in the treatment of cancer by tuberculin does not bear directly on the relationship of the two diseases, for the effect of the tuberculin may be due to the fact that it is a toxic substance and not to its derivation from the tubercle bacillus.

4 Statistical studies have been inadequate until recently, and the two most recent and best disagree in their conclusions.

5 Statistical analysis of the autopsy records of the Department of Pathology of the University of Michigan, when properly controlled, shows that active tuberculosis occurs neither more nor less frequently combined with malignancy than it does combined with any other major disease capable of producing death. Healed tuberculosis occurs with approximately equal frequency in cancerous and non-cancerous individuals.

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## Editorials

### CANCER AND TUBERCULOSIS

The view that there is an antagonism between cancer and tuberculosis is probably due chiefly to the teachings of Rokitansky, who wholly on the grounds of an extensive gross pathological experience concluded that there was a definite antagonism between active, florid tuberculosis and cancer. He especially emphasized the fact that cancer is only rarely found at those sites where tuberculosis most frequently occurs, as the lungs, for example, and that conversely the most favorite sites of cancer as, for example, the esophagus, stomach, rectum and ovary, are only rarely the seat of tuberculosis. An extensive literature on this subject has followed Rokitansky, made up largely of reports of cases in which there was a coincidental tuberculosis and carcinoma, and numerous recent papers of this kind have appeared. Rokitansky's dictum has had the effect of stimulating pathologists to such reports of the coexistence of the two diseases. Statistical studies of autopsy material have also been frequently carried out with respect to this question, and the majority of these have decided in favor of the Rokitansky view of the infrequent coincidence of the two diseases in the same individual. Some of these studies advance the view that the disposition to cancer carries along with it a high resistance to infection in general, not only to tuberculosis,

but also to syphilis, malaria and leprosy. On the other hand a familial association of tuberculosis and cancer has been noted by several writers, but these observations are rejected by Pearl as being the result of inadequate statistical technique. The latter considers the evidence as set forth in the literature to be "conclusive, to an overwhelming degree, to the effect that florid active tuberculosis and cancer occur together only with the greatest rarity." As to the experimental evidence favoring this view, such is extremely meager, and consists chiefly in the altogether inadequate experiments of Centanni and Rezzesi. These investigators worked with a strain of mice highly resistant to infection with the tubercle bacillus, and a transplantable adenocarcinoma which had a virulence of about 100 per cent. Injection of a mixture of cancer cells and living tubercle bacilli produced no tumors. Simultaneous injections of these two materials separately in different parts of the body depressed the rate of development of the neoplasm, though in some cases only temporarily. Previous infection of the animals with tubercle bacilli delayed the development of the subsequently inoculated tumor. Injection of the bacilli into an already growing tumor partially destroyed it, but some of the animals died with toxic symptoms. Dead tubercle bacilli had no influence in parallel experiments. Tuberculin mixed with the

tumor emulsion retarded or inhibited growth. They attributed their results to an allergic reaction against neoplasm, caused by the tubercle bacilli. Directly opposed to the observations made by Centanni and Rezzesi is the experimental work of Cherry (1929) who studied the development of spontaneous neoplasms occurring in a tuberculosis-resistant strain of mice. In such mice inoculated with living tubercle bacilli, he found that neoplasms occurred spontaneously much more frequently than in those not inoculated. On the grounds of a statistical study of 816 autopsies on patients having malignant tumors in the Johns Hopkins Hospital, and a case-for-case control series not having cancer or any other malignant tumor, Raymond Pearl found that active tuberculous lesions were found at autopsy in only 6.6 per cent of 816 persons with malignant growths, and in 16.3 per cent of 816 persons without malignant tumors. In 886 persons with active florid tuberculosis there were but 11 cases of malignant tumors, or 1.2 per cent of the total number. On the other hand, in 886 persons with no recorded tuberculous lesions at autopsy, of the same age, sex and racial distribution, there were 82 cases of malignant tumors, or 9.3 per cent. On the basis of these findings, Pearl concludes that there is a definite and marked incompatibility or antagonism between the two diseases, cancer and tuberculosis, of such sort that both occur together at the same time in florid activity in the same individual only with great rarity. This conclusion would not have been so bad, and would have passed only for an interesting statistical excursion of the

usual degree of value, had not Pearl been bitten by the flea of therapeutic application of these statistical results, as to the treatment of malignant tumors in human beings with some form of tuberculin. In connection with Sutton such treatment has actually been undertaken, with the following statement, as to results: "All that can be said at the present time is that in the cases treated the longest the tumors have shown definite retrogression. And the general condition of these patients is sufficiently encouraging to warrant our continuing the work, but a long time must pass before any final report can be made." A serious matter this, of arousing, even in the slightest degree, futile hopes of a possible cancer cure, in the many unhappy victims of malignancy, only too eager to grasp at any straw in the way of therapy. Futile—because of the lack of any positive evidence that such treatment will do anything more than to cause a possible temporary regression of the older parts of the neoplasm, produced not through any biologic antagonism between the two diseases, or the result of any constitutional differences, but wholly through the toxic action of the tuberculin, an effect comparable to that produced by the Coley's mixture of toxins—and nothing more than that. Further, Pearl is hoisted by his own petard of "inadequate statistical technique." Carlson and Bell in reporting a study of autopsy material similar to that of Pearl, found also that active tuberculosis was more common in the non-cancerous individuals than in those with some form of malignancy, while healed tuberculosis occurs with about equal frequency in both groups. But as

Carlson and Bell point out there is a serious objection to the use of a group as controls in which all manner of diseases were instrumental in causing death. They have demonstrated that a similar apparent antagonism can be demonstrated between heart disease and malignancy, and between heart disease and tuberculosis. And for that matter between tuberculosis and deaths from automobile accidents<sup>1</sup>. Further, Fortune in this issue, gives another statistical study of the association of tuberculosis and cancer, using a somewhat different method of control, as reference to his paper will show. The evidence from his statistical study likewise fails to establish the existence of any positive antagonism between the two diseases. The fact that healed tuberculosis is found with equal frequency in cancerous and non-cancerous individuals shows that a past infection is without any bearing on the development of malignancy. The statistics presented by both Carlson and Bell, and Fortune do not offer any support to the view that the person with active tuberculosis is less apt to have a malignancy, because of an immunity to cancer. He is less apt to have cancer, only because he usually dies of his tuberculosis before he reaches the cancer age. The coincident occurrence of the two diseases appears to follow closely the coincident occurrence of tuberculosis with other serious diseases capable of causing death. Active tuberculosis occurs neither more nor less frequently combined with malignancy than it does with any other

major disease capable of producing death. Healed tuberculosis occurs with equal frequency in cancerous and non-cancerous individuals. Pearl would have been more fortunate had he developed Beneke's conception of constitutional differences between those predisposed to malignant disease and those predisposed to tuberculosis. That there exist a heredo-neoplasia constitution and a heredo-tuberculosis constitution there can be but little doubt. The patient with the latter will usually succumb to his constitutional fate before reaching the carcinoma age. There is no reason why a hybrid of these two constitutions may not exist in the same individual, and there is abundant evidence to prove that such do occur. The existence of special constitutional susceptibilities to the two diseases does not mean that any biologic antagonism exists between the two processes. There appears to be, on the other hand, some evidence for the existence of a definite familial relationship between the two diseases. In certain families showing a family susceptibility to cancer in those who live to the cancer age, a very high mortality of the younger members of the given family from tuberculosis has been repeatedly observed. Whether there be any positive relationship of the susceptibilities of the two diseases to each other, as may hereby be indicated, the general fact remains, in explanation of the autopsy infrequency of their coincidental association, that the tuberculous die young, before attaining the age of malignancy.



## Abstracts

*The Epileptic Seizure Its Relation to Normal Thought and Action* By Joshua Rosett (Archives of Neurology and Psychiatry, April, 1929, p 731)

That epilepsy is a symptom-complex incidental to an abnormal functioning of the brain is an opinion advanced some thousands of years ago by Hippocrates, and from this opinion few, if any, dissent today. The discovery, however, of a large number of abnormal conditions, which by their action on the brain, may give rise to the disorder, compels a point of view from which the truth of the general proposition is seen in a new light. Every physician is impressed with the fact that out of a number of persons who have been subject to the same disease or accident, only a few become afflicted with epilepsy. Observations by Wilson, Hanptmann, Wallon and others, on the relation of war injuries to the causation of epilepsy, reveal the existence of predisposing factors in a large number of cases. The assumption that a disease or accident is potent in producing the disorder only when acting on an abnormal brain is indeed upheld by the study of its hereditary features. The latter, however, may be variously interpreted. Gowers' statistics, showing that a large proportion of epileptic patients are born of insane or epileptic antecedents, are upheld by the latest investigations. But all such statistics fail to give any information as to the nature of the particular defect in the parent which, when inherited by the child, makes the latter an epileptic. Thus, when one finds that of two persons who have received an equally heavy blow on the head, the one who in consequence became afflicted with epilepsy or insanity was the child of an insane or epileptic parent, we are still in ignorance as to whether the underlying cause of the disorder in both parent and child was due to some consti-

tutional defect acting on a normal brain, or to an essentially abnormal brain. Much light is shed on this difficult problem by certain discoveries. One is the discovery of the frequency of intra-ocular and meningeal hemorrhages in the new born, and the second is the growing importance of metabolic disorders as a factor in epilepsy. Their significance of the deepest gloom is mitigated by their value as a warning of impending danger to the human race. There is strong probability that all neuro-heredity statistics, including those of epilepsy, are in a way misleading. It is impossible to prove the inheritance of a defective nervous system as such, generation after generation may be in possession of a defect consisting not only of a disproportion between the child's head and the mother's pelvis and pelvic organs, but of a defective correspondence between the special metabolism of pregnancy and the embryonic formation of the enormously complicated structure of the human brain. Even when epilepsy is apparently inherited from the father, it is unsafe to conclude that there is an inheritance of a defective brain rather than an inheritance consisting of a metabolic defect which by its action on the brain is the cause of epilepsy in both father and child. That the arts of obstetrics and gynecology are adequate to save a number of lives of both mothers and infants, and even to reduce the percentage of intracranial damage, is an established fact. But no rational person can doubt that these recently arrived arts must perpetuate defects by enabling defectives to survive and procreate. Whether the progress of the medical arts will outstrip and compensate for the increasing number of defectives in successive generations, or whether a point will be reached when the medical arts will be swamped by the number of defectives, only the future can show.

Epilepsy is a form of the tetanic state which has its origin in that normal inhibition of the sensory system which results in a release of muscular activity. The sensory and muscular manifestations of the epileptic seizure are not essentially different from the processes of normal thought and normal action. The feature which distinguishes the epileptic seizure from normal thought, imagery and muscular activity is an increased facility and generally a greater degree of nerve inhibition. If the wave of inhibition extends only a short distance along the sensory pathway and recedes before completely extinguishing the function of the association systems, then such a minor seizure is devoid of muscular manifestations. If the wave of inhibition, in both the epileptic seizure and the process of thought, extinguishes all or a part of the highest portion of the sensory pathway—the association systems of the cerebrum—then the function of the efferent systems become manifest to a corresponding extent. The mechanisms of posture may be observed in the epileptic seizure to manifest their function before those of movement. The convulsive postures and movements of the epileptic, when reviewed in the prone position of the patient, appear to be irregular and absurd. Judged, however, as though the patient were in the upright position, they are unmistakably postures and movements which are integrated into normal patterns of muscular co-ordination. Outside of the occasional tremors and twitches which cannot be accounted for in the present state of knowledge, the movements are organized into complete and familiar acts which are frequently characterized by a considerable degree of beauty and grace. So varied are the acts of the convulsion in different individuals that it is not an exaggeration to say that there is hardly a normal posture-movement which is not represented in the convulsion of the unconscious epileptic. The various integrated movements of the epileptic convulsion, however, do not have reference to any co-ordinated acts which the person may have learned to execute in his conscious state. As a matter of fact, the convulsive

acts are such as the conscious epileptic is unable to repeat on request. The patterns of the co-ordinated movements and postures of the convulsion must, therefore, be inherent in the person's nervous system. Since the almost infinitely varied acts of the convulsion are not essentially different from normally integrated movements and postures, one may conclude that in normal persons the patterns of posture and movement which are integrated into discernibly separate acts are inherent in the nervous system. Other things being equal, the ultimate success or failure of a course of training in the execution of any skilled act must, therefore, depend on whether the particular posture-movement patterns exist or do not exist in the nervous system of the particular person. The detailed records of the various stages of the epileptic seizure show that the more profound the inhibition of the sensory system, the greater is the strength of the muscular contractions. The conclusion is therefore justified that a given degree of muscular contraction is normally conditioned by a corresponding degree of sensory inhibition. In the cases observed in this study, no change of a given posture-movement pattern could be produced by stimulation of the peripheral receptors. The amount of afferent nerve function remaining in the unconscious epileptic patient during the convulsion must therefore be less than in the animal decerebrated by a section at the highest level of the midbrain. If the epileptic seizure is a form of the tetanic state which is distinguished from normal processes of thought and action merely by an increased facility of inhibition of the nerve pathways, then it must be subject to the same laws of training to which normal mental and muscular function is subject. Experiments on animals show that a tolerance for the tetanic state can be acquired by training, even when the defect is as definite as the want of parathyroid influence. That an increased tolerance for the tetanic state can be acquired by a certain course of training in human beings is also shown by the experiments on epileptic patients in connection with the present work. Although the method employed in these experiments is,

on account of its great difficulty, impractical as a treatment for epilepsy, it is nevertheless suggestive of a certain line of education. The particular line to be pursued, however, must be left to the devices of the specialist.

*A Tentative Classification of the Forms of Chronic Splenomegaly of Unknown or Uncertain Origin* By J W McNee (Glasgow Medical Journal, May, 1929, p 288)

While at the present time no adequate clinical differentiation between the various forms of chronic splenomegaly is possible, a classification of an imperfect kind, based on differences in pathological anatomy and histology, has been attempted. The question of how far bacteriological methods may influence classification, and whether, for instance, aspergillum-like organisms are of etiological importance, is left open for further investigation. McNee's classification of chronic splenomegaly of unknown or uncertain origin is, as follows:

- 1 Splenomegaly with peri-ellipsoidal hæmorrhages and nodular siderosis (? splenic mycosis)
- 2 Chronic hemolytic (acholuric) jaundice
- 3 Thrombo-phlebitic splenomegaly
- 4 Chronic splenic hypertrophy, with or without fibrosis
- 5 Bantist's disease *Rare*
- 6 "Reticulo-endotheliosis" of the spleen
  - (a) slight (? chronic infections), or marked
  - (b) lipoidal group, diabetes, etc
  - (c) Gaucher-Pick-Niemann group
  - (d) tumors
- 7 Undetermined group
  - (?) chronic aleukemic leukemia
  - (?) primary lymphadenoma of spleen, and others

The history of our knowledge of the spleen and its diseases has been one of very slow development. One important fact going far back in the history of medicine is the knowledge that this organ is not necessary to life. Its structure, especially the finer histological details, has been imperfectly known and has recently been investigated anew. Old facts concerning the ellipsoids and the cellular arrangements of the organ

have been brought again to notice and new interpretations placed on some of them. The physiology of the spleen has been investigated from new angles by Barcroft and his colleagues, and the fruits of this work have not yet been fully gathered. Some of the diseases of the organ, such as those due to the parasites of syphilis and malaria, are easily understood, while even in some general diseases of unknown etiology, such as lymphadenoma, the histological changes and chronic enlargement of the organ can be rationally explained. There has remained hitherto a large group of cases of splenomegaly of quite unknown or of uncertain origin to which for the moment the term chronic splenic anemia is perhaps most suitably applied. No clinical classification of these cases is yet possible, but an attempt has been made to separate into groups, on histological grounds, a very large series of spleens which have been available for examination. The rough and entirely tentative classification, as given above, has been made, the shortcomings of which are obvious, but which may serve as a basis on which to build.

*Current Studies of Undulant Fever* By H E Hasseltine (Public Health Reports, July, 1929)

The first case of Malta fever in the United States was reported by Craig twenty-four years ago, who prophesied that a careful differential study of the obscure continued fevers prevalent in this country will result in the demonstration that Malta fever is by no means a rare disease in the warmer portions of the United States, and that many of the so-called anomalous cases of typhoid fever are in reality instances of infection with the micro-organism of Malta fever. This was practically forgotten until the disease was recognized by Perenbaugh and Gentry in the goat-raising sections of Texas, and even then it was considered only of passing interest. In 1917 Evans called attention to the fact that the organism causing Malta fever was practically identical with that causing infectious abortion of cattle, and in 1924, Keifer reported a case of Malta fever in man which was proved by

positive blood culture to be due to the abortus organism. Since 1926, each year has brought an increasing number of reported cases. As to the amount of undulant fever in the United States there are no reliable statistics. Information collected up to January 1, 1929, showed that 40 States reported 560 positive agglutination tests in 1928, 18 States reported 194 positive in 1927, and in 1926, 7 States reported 34 positive. Over 300 clinical cases of the infection have been reported in the literature since January 1, 1927. It is not known how many cases have passed unrecognized, or recognized and not reported. Among the diseases that may be confused with undulant fever are typhoid and paratyphoid fever, tuberculosis, rheumatism, malaria, influenza, focal infections, sinusitis, appendicitis and tularemia. The first symptom usually is a general feeling of weakness in the afternoon, accompanied by headache, or general aching. The patient then discovers that he has fever, which is usually preceded by chilliness, or a definite rigor, followed by a hot stage and a rather profuse perspiration, particularly noticeable upon awakening. When questioned closely, most patients report that the sweating is limited to the upper half of the body. It is quite common for patients to feel so well in the morning that they want to go to work, but if they do, they are ready to quit early in the afternoon. When seen in the febrile stage the patient appears only slightly ill, and if his temperature is taken, it will be surprising to find it 1-3 degrees higher than the general appearance of the patient would indicate. The daily variation is usually marked, being at or near normal in the morning, and going to 102° or 104° in the afternoon. If taken every four hours, a rather irregular curve within the day is frequently noted. The blood picture usually shows a slight anemia, a slight leucopenia and a considerable increase in the lymphocytes, with a corresponding reduction of the polynuclears. After the fever has risen by irregular steps to a maximum of 103-104°, occasionally higher, it usually declines by lysis, and remains normal for a period vary-

ing from three days upward. Then another febrile wave begins, usually not quite so severe, nor quite as long as the first, followed by an afebrile wave slightly longer than the first. Some cases have but one febrile wave, others have them irregularly over a period of one to three years. The general symptoms of the disease come and go with the febrile wave. Joint pains, especially upon getting about after the fever has returned to normal, are present in most cases. They vary from slight pain to moderate interference with the function of the joints. Anorexia, constipation, insomnia and increased irritability are present in a majority of cases. The most prominent complications reported have been orchitis or epididymitis, and abdominal conditions, caused by a localization of the infection in the viscera, particularly in the female reproductive organs. Prostatic symptoms have been noted in the male, and abortion in pregnant women has been attributed frequently to this infection. It is too early to know whether the infection may cause any later sequelae, such as sterility, which the disease is known to cause in some of the domestic animals that it attacks. Comparatively little is known of the pathology of the infection in human beings. Whether the infection with the types of *Brucella abortus* differs in its pathology from that of *Brucella melitensis* is not yet known. For diagnosis, blood serum should be submitted for an agglutination test against *Brucella abortus* as well as against the typhoid organism. A positive agglutination test in 1:80 dilution, or higher, in a case presenting the symptoms of undulant fever warrants a diagnosis even in the absence of positive blood cultures. The obtaining of blood cultures is important in order that the strain of the infecting organism may be determined. At the present time, it appears that there are at least three strains of the *Brucella* germs that may cause undulant fever, the caprine, bovine, and porcine strains. The exact relationship of these strains to human undulant fever remains to be determined.

## Reviews

*Recent Advances in Cardiology* By G F Terence East, M A (Oxon), F R C P (Lond), Junior Physician, King's College Hospital, Physician, Woolwich Memorial Hospital, Sometime Radcliffe Travelling Fellow, University College, Oxford, and G W Curtis Bain, M C, M B (Oxon), M R C P (Lond), Assistant Physician, Harrogate Infirmary 342 pages, 12 plates and 57 text-figures P Blakiston's Son & Co, Philadelphia, 1929 Price in cloth, \$3 50

This volume is one of the "Recent Advance Series," and attempts to give a summary of the new knowledge of the last twenty-five years regarding the heart and circulation. It makes an appeal, both to the older practitioner who wishes to become conversant with the latest ideas, and also to those who seek special knowledge upon cardiac subjects. It, therefore, embraces both the practical and academic aspects of cardiology. Throughout the book the electrocardiogram has been considered as part of the clinical picture. The majority of the references are to work of the last decade. While in a book so limited in size adequate abstracts of the work referred to cannot be given, the book still covers the ground of modern cardiology very thoroughly. Few important modern contributions to this subject have been missed. The electrocardiographic illustrations are very good. The book is well printed, and the material and discussions are very good. It will be useful to the general interest as well as to the specialist in cardiology.

*Sterilization for Human Betterment* By E S Goss, B S, I L B, and Paul Popenoe, D Sc. 202 pages. The MacMillan Company, New York, 1929. Price in cloth, \$2 00

This is a public publication of Human Bet-

terment Foundation, and gives a summary of 6,255 operations for sterilization performed in California, 1909-1929. There were 601 more males than females sterilized, 1,488 were on feeble-minded, and in this group there were 330 more females than males. All feeble-minded patients are now sterilized before they are allowed to leave the state home at Sonoma. One in twelve of all the insane admitted to the state hospitals since the law was passed has been sterilized. One in five or six of the new admissions is now sterilized. Sterilization is done only where there is danger of defective children. This book reviews the effects of the operation as carried out in California, and gives a general discussion of the various aspects of the problem. It is written in popular language, and in a clear simple style. It is an excellent presentation of the subject from all standpoints, and should be read by all thinking citizens. The chapters on "Sterilization for Social Reasons" and for "Eugenic Reasons" are particularly useful to the ordinary reader in helping him to formulate his opinions as to the justification of sterilization. The general text is followed by a number of valuable appendices. This book cannot help but clarify the subject in the minds of all who read it, and this is a manner upon which all thoughtful citizens, medical as well as lay, should be fully informed.

*An Introduction to the Study of Physic* [Now for the First Time Published] By William Heberden [1710-1801]. A Prefatory Essay by LeRoy Crummer. With a Reprint of Heberden's "Some Account of a Disorder of the Breast." 159 pages, portrait in photogravure, 6 illustrations. Paul B Hoeber, Inc, New York, 1929. Price in cloth, \$2 00

This unpublished original manuscript of Heberden was a lucky find by Dr Crummer.

in a little second-hand book shop in the south of London. Picked up as a medical manuscript in Wales the week before by the book-seller, the volume handed to Dr Crummer had written on the title-page "An Introduction to the Study of Physic," and beneath this the signature "William Heberden." We may be sure that this was an exciting moment in the book-collector's life, and he tells us that when he left the shop the manuscripts were safely under his arm. Then followed the excitement of identifying the signature as being actually Heberden's, and of the discovery that the manuscript represented a hitherto unpublished work of Heberden. All of this is told by the author in a most interesting manner calculated to excite an answering thrill in all other collectors who may read this prefatory essay. When compared with the manuscript of Heberden's "Commentarii" in the Royal College of Physicians, the manuscripts found by Dr Crummer proved to be identical with the former in paper, quire arrangement, format and the limp vellum binding, as well as in the beautiful script of William Heberden. In one of the volumes found there is written on the recto of seventy-four pages the manuscript of "An Introduction to the Study of Physic." There is no date recorded in the manuscript, nor any direct citation of current events which would definitely place the year or years of its composition. Crummer thinks that it must have been written in the latter part of Heberden's Cambridge period, or at least in the early years of his life in London (1744-1755). He thinks it fair to assume that the original idea was formed while he was teaching at Cambridge, that the material was finally revised during his early years in London, and that the final form represents Heberden's plan for a proper arrangement of the medical curriculum at the end of his experience in teaching in Cambridge. This period was a very significant one in the history of English medicine. A general dissatisfaction in medical education was manifest in different quarters. Edinburgh was just beginning its brilliant career as a primary center of medical education. Written at such a period the "Introduction" may be regarded from

two standpoints, the purely personal and the other, as an exhibit hitherto unrecorded in the general history of medical education. It would seem that in the "Introduction" Heberden has given an autobiographic survey of his own method of study, a list of the authorities in his judgment most worth while, and a criticism of antecedent medical literature based on an unequalled understanding of original texts. His comments on the latter became authoritative, as from one who had a complete understanding of the state of the medical sciences of the time, as well as an extraordinary ability in the languages used in the originals. The test of time has to a great measure justified his choice of authorities. He mentions one hundred and fourteen books. He insisted upon the importance of studying source literature, his chapter on anatomy with few changes would hold its place in one of the great educational arguments of the present time. Had Heberden elaborated the ideas expressed in this manuscript, medical education might have been advanced a full century. The manuscript has been printed without change or emendation. The volume closes with a reprint of Heberden's "On a Disorder of the Breast," the classic report on Angina Pectoris. The book is beautifully printed, and is to be counted as another of Hoeber's successful achievements in medical history publication. It should be in every one's collection.

*Applied Electrocardiography* By A. E. Parsonnet, M.D., F.A.C.P., Attending Physician and Cardiologist, Beth Israel Hospital, Newark, N.J., and A. S. Hyman, A.B., M.D., F.A.C.P., Associate Physician and Cardiologist-in-Chief, Beth David Hospital, New York. With a Foreword by Harlow Brooks, M.D., F.A.C.P., Professor of Clinical Medicine, New York University. 206 pages, 120 illustrations. The MacMillan Company, New York, 1929. Price in cloth, \$4.00.

No mechanism of the entire mammalian make-up has aroused more speculative interest among physiologists and anatomists than that of the heart. With each succeeding generation there has come out some new

device or method whereby greater knowledge of the heart's action could be obtained by the practicing physician. Thus have appeared in succession the stethoscope, blood-pressure apparatus, the art of percussion, the polygraph, and lastly the electrocardiograph, all serving to present to the physician new and better information in regard to the functional integrity of the cardiovascular system. So detailed and so complex has become the information about the heart, derived from these various methods of examination, that the physician today stands confused and perplexed when confronted with the problem of examining the heart at the bedside. The authors recognize full well the apprehensive attitude displayed by most physicians at the mere mention of the word electrocardiogram, and it is their hope that this volume may dispel that inferiority complex that surrounds the physician when contemplating the use of the electrocardiograph. This book is written for those practitioners who have neither the time nor the scientific make-up needed for a thorough perusal and contemplation of the extensive literature on electrocardiography. An attempt is made in it to reduce the knowledge amassed by the pioneer investigators in this field to simple truths, essential in the every day experience of the practicing physician. No apology is made for the attempt to present problems of the utmost scientific abstractness in terms of bedside simplicity. Highly problematical and debatable hypotheses are omitted. Free use is made, however, of the established phraseology of the cardiologic laboratory in the belief that the terms employed to describe electrocardiographic findings will soon become an integral and familiar part of the physician's vocabulary. The authors have selected typical graphic records of the common diseases of the heart, and have taken advantage of their rich supply of records obtained from thousands of cases. The theory and application of electrocardiographic technique has been so simplified that the interpretation of graphic heart records is made easily available to every practitioner of medicine. The book is designed for the education of the practitioner in the

art of interpreting the clinical features of his cases. It is a book written by clinicians for clinicians rather than by physiologists or technicians. In this respect it fills a definite need.

*Otosclerosis*. A Resumé of the Literature to July, 1928. Compiled under the Direction of the Committee on Otosclerosis, American Otological Society, Nowal H. Pierce, M.D., Eugene A. Crockett, M.D., James F. McKernon, M.D., J. Gordon Wilson, M.D., J. Gordon Wilson, M.D., Arthur B. Duel, M.D., Editor. Volumes I and II. 684 pages with indices. Paul B. Hoeber, Inc., New York, 1929. Price in cloth, \$15.00.

The Committee appointed by the American Otological Society, in 1925, undertook to make a complete resumé of the literature on Otosclerosis. These volumes present the results of this work. Any comment on, or criticism of, the subject matter has been purposely avoided. The resources of the largest libraries in the United States—the Surgeon-General's Library and the Library of the New York Academy of Medicine—have been used in the compilation of this work. Its chronological arrangement shows the development of our present knowledge and understanding of otosclerosis in all of its phases. Not only are the pathological findings of various investigators presented in detail, but also the numerous theories as to its etiology and the other phases of the subject that are still open to discussion. No other such comprehensive survey of the literature on this subject has thus far been published. It shows what is actually known in regard to otosclerosis, and suggests the wide fields that are still open to scientific investigation and research. Here is presented a wealth of material which is otherwise available only in widely scattered form and places, in many different languages, and in many inaccessible journals. This volume brings to the otologist all the available data on otosclerosis in an easily usable form. Every otologist, whether research worker or practitioner, needs to be familiar with the survey, so that he may know what is, and what is not, established fact in regard to oto-

sclerosis, its pathology, etiology, diagnosis and treatment. This compilation was carried on as part of a program of research in otosclerosis which the American Otological Society began in 1925, under a grant of \$90,000 made by the Carnegie Corporation. This subsidy, extending over a period of five years, was awarded in amounts decreasing each year, with the expectation that the Society could build up an independent fund to expound and carry on the work. A campaign to secure a permanent endowment fund of \$2,500,000 is now under way. The Scientific Committee of the Otological Society plans first to investigate the chronic progressive types of the disease. Later the

research will be extended to other otological problems. The contents of the two volumes are arranged as follows: Volume I, Preface, Section I, Pathology, Stapes Ankylosis, Changes in the Labyrinthine Capsule, Section II, Etiology, Heredity as an Etiological Factor, Congenital Conditions in the Labyrinthine Capsule, Influence of Local and General Conditions. Volume II, Section III, Symptoms and Diagnosis, Section IV, Treatment. There are appended full bibliographies and indices. No otologist can afford to be without these two volumes with their complete resume of all our knowledge on this important subject.



## College News Notes

### THE MINNEAPOLIS SESSION of THE AMERICAN COLLEGE OF PHYSICIANS

S. Marx White, M.D., General Chairman  
of Arrangements

Preparations for the Minneapolis meeting of the College during the week of February 10th are well advanced. The program already under way has a character and content to lure every member, Fellow or Associate as the case may be, and to attract as well a great number who may be thinking of affiliation with the College or who may be interested only in the scientific material presented. Details of the Scientific Session and of the Clinics will be given in a later issue of the ANNALS. A glance meanwhile at the setting should be of interest.

Minneapolis lies, as the Mississippi River flows, about five hundred miles from the source of the Father of Waters, and nearly two thousand miles from its mouth in the Gulf of Mexico. It has been made, by vast engineering works, the head of navigation of this waterway and will soon be of even greater importance in the transportation system of the Valley and of the nation.

There was a time not so long ago when the waterway was the most important means of transportation to the inland empire centering here and brought the famous voyageurs and missionaries to the neighborhood of St. Anthony Falls. Points of interest, avenues and institutions commemorate the names of Hennepin, Nicollet, Radisson and Marquette. Joliet, Grosvenor, La Perriere and Le Sueur began their journeys of exploration here. McLeod, the site of Sibley House, the first house built in the territory, lies about seven miles down the Mississippi River from the heart of Minneapolis. Here the Mississippi River joins a

larger Mississippi and here also, a mile nearer, stands historic old Fort Snelling, guarding the meeting point of the two ancient waterways.

Minnesota is the Land of Ten Thousand Lakes. Minneapolis, the larger of the Twin Cities, is a city of lakes and parks, homes and gardens. Within the city limits are ten lakes, six of them of large size. All are public property, having been acquired early by men of vision on the Park Board. About these lake parks are grouped some of the finest residence districts to be found anywhere. There are in all 131 public parks and playgrounds, the largest Glenwood Park, including 681 acres of groves, gardens of wild flowers, municipal golf links and bathing beaches. Here is a gigantic ski slide for winter sports. Skating, outdoor hockey and horse racing on the ice are amply provided for on Lake of the Isles. Commodious and comfortable enclosed hockey rinks provide the public with opportunity to witness this dashing sport.

The City of Minneapolis was chartered in 1854, and recently celebrated its 75 anniversary. Today the population exceeds 500,000, and one million people reside within a radius of 25 miles. Men of vision and power were its founders and to these, coupled with its strategic location, are due its tremendous growth and influence. The lumbering industry, once of prime importance,

as well as the invitation of the makers of the flour thus advertised. The leading industries include printing and publishing, general construction, and the manufacture of motor vehicles and parts, structural and ornamental iron, mill-work and other lumber products, heat regulators, foundry products, linseed oil, cake and meal, knit goods, bakery products, flour, breakfast foods and other food necessities.

The public school system is said to be one of the best in the country. The Minneapolis Public Library has twenty branches and fifteen stations. Illiteracy claims only 12 per cent of the population, a figure said by those who know to be the lowest among the larger cities of the United States.

In point of size, the University of Minnesota is among the first five in the country. In 1928-29 it registered 16,713 students. The same year the Medical School registered 751 graduates. The Graduate School of the University supervises all graduate work, including that for advanced degrees in medicine and its specialties, both on the main campus in Minneapolis and at the Mayo Foundation in Rochester, ninety miles away.

The main campus of the University lies in a great bend of the Mississippi, in the south east section of the city, and can be reached in a few minutes from the principal hotels, as well as from the Auditorium, where the Scientific Assembly will be held. It covers twenty-four city blocks and the newer portion is in a pleasing style of architecture on a comprehensive plan by Cass Gilbert. Built in this newer style, the Medical School and University Hospitals occupy a commanding site with an inspiring view down the great gorge in which the river lies. To the Elliott and Todd Memorial Hospitals and the Cancer Institute have just been added the Eustis Hospital for Children, a new general pavilion with improved quarters for the Out-patient Department, and a new hospital and dispensary for the Students' Health Service. These additions will all be in operation by the time the College meets in February.

The laboratories of the State Department of Health are on the campus near the

Medical School and provide added facilities for instruction in Public Health.

Beside the University Hospitals, twelve hospitals, most of them of major importance in the health and life of the city and its territory, are to be utilized in the Clinics of the session. Most important in this group is the Minneapolis General Hospital, with more than 600 beds, under a progressive and able Superintendent, a medical man whose work in this field has been notable.

Glen Lake Sanatorium, the Hennepin County institution for the tuberculous, located in a suburb of Minneapolis, but readily accessible from the Auditorium, has over 700 beds and is one of the largest and most modern institutions of its kind. Students from the University Medical School obtain instruction in tuberculosis, during stated periods of clerkship, under a permanent and visiting Staff whose work has attracted country-wide notice.

The campus of the Agricultural School is three miles from the main University Campus and lies within the city limits of St Paul. Here may be found laboratories where outstanding work in chemistry, animal husbandry and horticulture is going on. Some of this work is of immediate interest to the physician and will be demonstrated during the scientific sessions.

Minneapolis is a center of culture for the Northwest. In the Art Institute have been gathered masterpieces of painting and sculpture, rare and notable tapestries and objects of art. There are larger collections in the great centers of the country, but the discrimination shown in selection and the taste used in display have called forth favorable comment from authoritative critics.

The Walker Art Gallery, provided and furnished by the late lumber baron, on a unique and centrally located site, gives an opportunity for viewing old masters' miniatures, ancient jewelry and jades, as well as Greek, Egyptian and Chinese pottery, comprise a collection of peculiar character and interest.

The Minneapolis Symphony Orchestra has carried the name of the city to music lovers from coast to coast through its annual tour. Great schools of music and the

arts have their homes in the commonwealth. The theatres are adequate and provide a variety of entertainment agreeable to every taste.

From the the wealth of material presented for study by this stately and yet charming city of the Northwest, soon to be our host, it has been possible to select only a few features for comment. The Municipal Auditorium might be described in extensive detail, for it has already proved to be the most suitable and attractive of meeting places for a session such as the one to be held during the week of February tenth. Whole blocks of buildings have been razed to provide a proper view and approach. The location is convenient to the hotels. When the Auditorium is to be used for one great meeting place, more than 15,000 people can be seated, and from any point vision and hearing are perfect. For the Scientific Assembly of the College, a suitable space at the stage end of the great structure will be walled off by immense, sound-proof curtains. Thus a comfortable hall is provided, with adequate seating facilities and protection from disturbing noises. Every device for the illustration of papers and the demonstration of specimens will be furnished. Before entering the hall of meeting, the visitor finds himself in a spacious and commodious lobby, where registration goes on with dispatch and ease, where all the exhibits will be suitably housed, and where the amenities may be practised at all hours when the attractions of the session are not too impelling.

The Auditorium will not, this time, be the center for making appointments for golf, fishing or canoe trips. Note carefully the date, which was specifically requested by the Fellows from the South. The Auditorium, the hotels and the homes, as well as the cars and taxicabs of Minneapolis, however, boast of a more comfortable temperature in February than one has ever been able to find in that same month in Southern California. Come to Minneapolis in February and find a wealth of scientific lectures, as well as a plethora of interesting classes and demonstrations in the various fields of biology, chemistry, physics, geology, and astronomy. The scientific

profession. If you have no friends there now, you will be sure to make them when you come. Bring your overcoat, or if you have none, come anyway and borrow one for the wealth of this metropolis of the Northwest is so great that every citizen of Minneapolis has at least two.

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A postgraduate course for the benefit of general practitioners was inaugurated last September by the Medical Staff of St Michael's Hospital, Toronto. The Fellows of the College who addressed the meetings and conducted clinics were Drs J H Elliott, J D Loudon, H McPhedran, A J McKenzie, E A Broughton and F C Harrison.

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Dr Lewellys F Barker (Fellow), Baltimore, is the first occupant of the newly established visiting professorship in the Medical School of the University of California. Dr Barker will deliver a series of lectures and conduct clinics at the California institution during March, 1930.

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Dr James S McLester (Fellow), Birmingham, Ala., and Dr Charles C Bass (Fellow), New Orleans, will deliver addresses before the Issaquena-Sharkey-Warren Counties (Miss.) Medical Society at its December meeting.

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Dr Ralph Pemberton (Fellow), Philadelphia, and Dr Logan Clendenning (Fellow), Kansas City, were speakers at the Kansas City Annual Clinical Conference, October 7-11.

Dr George T Harding, Jr (Fellow), Columbus, addressed the Pickaway County (Ohio) Medical Society at Circleville, August 2, on "Hobbies and Specialties" in the practice of medicine

Dr Henry L Bockus (Fellow), Philadelphia, delivered two addresses before the joint meeting of the Jackson County (Mo) Medical Society and the Kansas City Southwest Clinical Society, September 10. His subjects were "Syphilis Associated with Pathology in the Upper-Gastro-Intestinal Tract" and 'Duodenal Stasis"

Dr Ray M Balyeat (Fellow), Oklahoma City, is President of the American Society for the Study of Allergy

Dr E C Thrash (Fellow), Atlanta, gave a report of the Portland session of the American Medical Association before the Fulton County (Ga) Medical Society on August 1

At the twenty-sixth annual meeting of the Nevada State Medical Association, (low), Rochester, Minn, and Dr Albert Sept 27-28, Dr Howard R Hartman (Fellow), Los Angeles, Calif, spoke on "Medical Treatment of Ulcer of the Stomach and Duodenum" and "Carcinoma of the Breast", respectively

Dr James Allen Jackson (Fellow), Danville, Pa, addressed the Montgomery County (Pa) Medical Society at Norristown, September 4, on mental hygiene

Dr Stuart Graves (Fellow), University, Ala, has been appointed acting health officer of Alabama by the State Board of Health, during the absence of Dr Douglas L Cannon, who has been ill for some time

Dr Edwin Schisler (Fellow), St Louis, Mo, addressed the San Diego County (Calif) Medical Society on heart disease, September 10

Among speakers at the 109th annual meeting of the Michigan State Medical Society at Jackson, September 17-19, were the

following Fellows of the College Dr William Gerry Morgan, Washington, D C, Dr William Englebach, St Louis, Mo, Dr Frederick A Willius, Rochester, Minn, Dr George E Brown, Rochester, Minn, Dr Frederic W Schultz, Minneapolis, Minn

Dr Arthur C Morgan (Fellow), Philadelphia, and Dr Edgar M Green (Fellow), Easton, were speakers at the opening of the newly reconstructed Portland (Pa) Hospital

Dr Colonel B Burr (Fellow), Flint, Mich, addressed the Oakland County (Mich) Medical Society, September 12, on "Professional Contacts and Near-Contacts"

Dr Hugh S Cumming (Fellow), Surgeon General of the U S Public Health Service, delivered an address before the sixtieth annual meeting of the Medical Society of Virginia at the University of Virginia, Charlottesville, October 22-24

Dr Horton R Casparis (Fellow), Nashville, Tenn, addressed the Central Tri-State Medical Society at Huntington, W Va, Sept 19, on "Treatment of Tuberculosis in Children"

Dr James D Bruce (Fellow), Ann Arbor, Mich, as councillor, with officers of Livingston, Lenawee, Monroe and Washtenaw (Mich) County Medical Societies, conducted a meeting of members of those societies at the state sanatorium at Howell, October 8. Dr Stuart Pritchard (Fellow), Battle Creek, conducted one of the clinics

Dr Guy L Kiefer (Fellow) Lansing, Mich, is the State Commissioner of Health

Dr James M Hutcheson (Fellow and Governor for Virginia), recently addressed the Northampton County (Va) Medical Society at Nassawadox, Va, on 'Heart Pains"

Dr William A Evans (Fellow), Detroit, and Dr James H Hutton (Associate), Chicago, were speakers at the 52d annual meeting and dinner of the Chicago Gynecological Society on October 11

Dr James Alex Miller (Fellow), New York City, was recently elected chairman of the Committee on Public Health Relations of the New York Academy of Medicine

Dr James E Paullin (Fellow), Atlanta, Dr Warfield T Longcope (Fellow), Baltimore, and Dr Walter L Bierring (Fellow), Des Moines, are among the trustees of the Frank Billings Lectureship Fund, established during the Minneapolis meeting of the American Medical Association by the Section on Practice of Medicine. The object of the fund is to provide a lecturer each year before the Section. Dr Bierring will be the Treasurer.

At the regular meeting of the North Pacific Society of Internal Medicine, on September 14, at Tacoma, Wash, Dr Charles F Sears (Fellow), Portland, Ore, was elected President and Dr Lester J Palmer (Fellow), Seattle, Wash, was re-elected Secretary-Treasurer. This Society was organized about three years ago and its membership is limited to forty physicians, whose practices have been restricted to the field of internal medicine for a period of at least five years. Several of its members have been elected to Fellowship in the American College of Physicians.

The following fellows of the College were on the program of the sixty-sixth session of the Homeopathic Medical Society of the State of Pennsylvania held at Philadelphia on September 24, 25, and 26. Dr Ralph Bernstein, Dr Carl V Vischer, Dr F Roland Snider Jr, Dr G Harlan Wells, Dr G Morris Golden. Dr G Harlan Wells of Philadelphia was chairman of the section on Clinical Medicine.

Dr H D Farland (Associate) Wood  
Dr C. H. ... is retired from active practice

Dr William R Dancy (Fellow), Savannah, Ga, is President of the Medical Society of Georgia. Dr Dancy was recently appointed a member of the Board of Judges (Georgia State Committee), by the American Chemical Society, to pass upon essays rendered upon this Society in competition for the prizes which it offers.

Dr Herman M Baker (Fellow), Evansville, Ind, has been highly commended for the successful arrangements made for the Indiana State Medical Association meeting at Evansville, September 25, 26, and 27. Dr R H Beeson (Fellow), Muncie, Ind, was chairman of the Medical Section and introduced the following Fellows of the College, who gave addresses: Dr Elliott P Joslin, Boston, Mass, "The Abolition of Diabetic Coma in the United States", Dr Francis Eugene Senechal, Chicago, Ill, "Cutaneous Tuberculosis and General Medicine", Dr Robert M Moore, Indianapolis, Ind, "Subacute Bacterial Endocarditis—Some Clinical Observations", Dr Walter Clement Alvarez, Rochester, Minn, "What Shall We do for the Patient With Nervous Indigestion?", Dr Ralph Pemberton, Philadelphia, Pa, "Arthritis". Dr Moore's paper was discussed by Dr Edgar F Kiser (Associate), Indianapolis. Dr Moore was elected chairman of the Medical Section for 1930.

Dr R H Beeson is President of the Muncie Academy of Medicine. At the meeting of the Academy, on October 2, Dr Larue D Carter (Fellow), of Indianapolis, delivered an address on "Chronic Encephalitis".

Lt Col W S Shields (Fellow), heretofore stationed at the Fitzsimmons Hospital, Denver, Colo, was recently transferred to Ft Sam Houston, Texas to relieve Col Roger Brooke (Fellow). He is chief of the medical service.

vama at its recent meeting Dr Snader is the author of an article, "A Modern Conception of Treatment of Cardio-Vascular Syphilis", in the September issue of the Hahnemannian Monthly

The Coney Island Hospital of Brooklyn, N Y, has recently undergone a reorganization under the direction of Dr William Schroeder, Jr, Commissioner of Hospitals of the teaching units of the Long Island It is reported that this Hospital will be one College Hospital Dr Philip I Nash (Fellow), has been appointed Chief of Medicine, Dr Thomas J Longo (Fellow), Attending in Medicine, Dr Judson P Pendleton (Fellow), Chief of Pediatrics, Dr Nation T Beers (Fellow), and Dr J M VanCott (Fellow), members of the Consulting Staff

Dr E Sanborn Smith (Associate), of Mo, and lecturer on Pediatrics in the Kirks-Grim-Smith Hospital and Clinic, Karksville, ville State Teachers College, has been placed on the State Board of Health by Governor Caulfield

Dr Carl V Vischer (Fellow), Philadelphia, is the author of a case report, "Chronic Ulcerative Colitis-Perforation and Peritonitis," which was published in the September number of the Hahnemannian Monthly

Dr John A Lichty (Fellow and Regent), at a recent meeting of the Seventh District Medical Society, held at the Clifton Springs Sanitarium & Clinic, Clifton Springs, N Y was re-elected Secretary of the Society for the ensuing two years Papers were read at the meeting by Dr L G Rowntree (Fellow) of the Mayo Clinic, Dr Edward Archibald of McGill University, Dr Louis Hamman of Johns Hopkins University, and Dr Frank A Kelly of Detroit

Dr C Harvey Jewett (Fellow), of the Clifton Springs Sanitarium & Clinic, on October 8, as President of the Ontario County Medical Society, presided at a dinner in celebration of his father's, Dr John H Jewett, fiftieth anniversary in practice in

this County Dr Jewett's grandfather and great uncle, doctors of the same name, have furnished a continued service of 110 years in the practice of medicine in this County The address of the evening was given by Dr J H VanderVeer, President of the State Medical Society of New York

Dr Joseph McFarland (Fellow), Professor of Pathology at the University of Pennsylvania School of Medicine, is the author of an article, "Heredity in Malignant Disease," in the October number of the Pennsylvania Medical Journal

Dr Herman B Allyn (Fellow) has resigned as Visiting Physician to the Philadelphia General Hospital, also as President of the Medical Board, and has accepted an appointment as Consulting Physician

Dr Noel F Shambaugh (Fellow) recently resigned as assistant professor at the University of Michigan to accept an appointment on the medical faculty of the University of Southern California Dr Shambaugh is now residing in Long Beach, Calif

Dr P P McCain (Fellow), Sanatorium N C, was elected President of the Southern Tuberculosis Association at its annual meeting in Nashville, Tenn, Sept 25, 26 and 27 Dr McCain served last year as President of the Southern Sanatorium Association

Dr Myer Solis-Cohen (Associate), Philadelphia, Pa, read a paper on "Tuberculin in Diagnosis and Treatment in Infancy and Childhood, With a Method for Determining the Appropriate Therapeutic Dose in the Individual Case" before the Section on Pediatrics of the Medical Society of Pennsylvania, at Erie, on October 1

Dr Solis-Cohen also read a paper with Dr Rachel Ash, on "The Action of Whole Fresh Blood upon Pneumococci before the Pathological Society of Philadelphia on October 10

Under the Secretaryship of Dr Harold Swanberg (Fellow), Quincy, Ill., the Adams County Medical Society of Illinois held its annual fall clinical conference at Quincy, October 14. The program was known as the "All-Philadelphia Program," since every speaker was selected from the faculties of the School of Medicine and of the Graduate School of Medicine of the University of Pennsylvania.

Dr Leroy H Sloan (Fellow), Chicago, addressed the Winnebago County Medical Society, Rockford, Ill., October 8, on "Fundamental Principles in Neurologic Diagnosis."

Dr Louis A M Krause (Fellow) Baltimore, Md., at the opening of the fall semester of the University of Maryland School of Medicine, was promoted to Assistant Professor of Medicine.

Dr Anton J Carlson (Fellow) and Dr Arno B Luckhart of the University of Chicago have produced a film showing the movements of the alimentary tract in experimental animals. This film was presented before the Omaha-Douglas (Nebraska) Medical Society on September 21.

Dr Nelson G Russell (Fellow), Buffalo, N. Y., has been appointed to the chair of professor of medicine in the University of Buffalo School of Medicine.

At the recent annual meeting of the Medical Society of the State of Pennsylvania at Erie, Dr William T Sharpless, West Chester, Pa., was elected President, Dr Ross V Patterson (Fellow), dean of Jefferson Medical College Philadelphia, was made president elect and Dr Alexander H Stewart (Fellow), Indiana Pa. was elected one of the vice presidents.

Dr Arthur C Morgan (Fellow), Philadelphia, Pa., addressed the Summit County (Ohio) Medical Society, Akron, October 8, on "The Treatment of Acute Cardiac Tragedies."

Dr Abraham H Aaron (Fellow), Buffalo, N. Y., addressed the Eighth District (Ohio) Medical Society, October 3, on "Gastro-Intestinal Therapeutics."

## OBITUARY

Dr Rudolph William Gelbach (Fellow), Hoboken, N. J., died at his summer home, Keene Valley, N. Y., August 2, 1929, of recurrent carcinoma of the kidney, aged 72.

Dr Gelbach was born in Pfalz, Germany November 30, 1857, was educated in the Universities of Strassburg, Munich and Würzburg, filled the compulsory term of military service by work in military hospitals, and received his medical degree from the University of Munich in 1881. He came to America in 1883, and for two years practiced in Mendota, Illinois. Coming to Hoboken, New Jersey, in 1886 to visit his parents, he was induced to help an older physician who was ill, and he was soon so busy that he abandoned his plan to return to Illinois and remained in Hoboken for the rest of his active life.

For many years, Dr Gelbach was visiting surgeon at St. Mary's Hospital, Hoboken, visiting physician at Christ Hospital, Jersey City, and consulting physician at North Hudson Hospital, Weehawken, and at the Farr Sanatorium, Hoboken. He was known throughout Hudson County for his skill in diagnosis and is said to have kept himself thoroughly conversant with all the methods of diagnosis and

treatment. He was always ready to assist other physicians in emergencies without thought of remuneration, his ready, spontaneous wit and humor made him a most agreeable associate.

During the last three years of his life, he gave up private practice and confined his work entirely to consultations. In October, 1927, he underwent nephrectomy, made a good recovery and was comfortable for over one year when recurrence in abdominal glands caused his death on August 2 of this year.

Dr. Gelbach's chief diversion was hunting, he had a wonderful collection of animal heads to show for his

tips. He hunted and brought game from the Rocky Mountains, Labrador, New Brunswick, Lower California, Mexico and Africa. In October, 1928, in spite of his depleted physical condition, he travelled alone in Spain, Italy, Sicily, Tunis and Egypt.

Surviving Dr. Gelbach are two sons, one daughter, one brother and three sisters.

He was a member of the New Jersey State Medical Association, the Hudson County Medical Society, the American Medical Association, the New York Academy of Medicine, and had been a Fellow of the American College of Physicians since 1920.

*Circulation*  
of  
*ANNALS OF INTERNAL MEDICINE*  
October, 1929

United States	2,135
Canada	56
Panama and the Canal Zone	8
Hawaii	4
Germany	3
Mexico	3
Porto Rico	3
Australia, Cuba, India and Philippine Islands (2 each)	8
Argentina, Belgium, Central America, China, Denmark, England, France, Haiti, Italy, Japan, Java, Roumania, Russia, South Africa and Switzerland (1 each)	15
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	2,235



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Arkansas	12	New York	277
California	142	North Carolina	20
Colorado	33	North Dakota	4
Connecticut	27	Ohio	120
Delaware	2	Oklahoma	26
Dist of Columbia	93	Oregon	19
Florida	15	Pennsylvania	223
Georgia	55	Rhode Island	7
Idaho	3	South Carolina	7
Illinois	110	South Dakota	1
Indiana	51	Tennessee	33
Iowa	24	Texas	71
Kansas	13	Utah	3
Kentucky	37	Vermont	2
Louisiana	42	Virginia	26
Maine	17	Washington	24
Maryland	45	West Virginia	30
Massachusetts	59	Wisconsin	47
Michigan	135	Wyoming	1
Minnesota	68		
Mississippi	10		2,135
Missouri	62		
Montana	7	October 16 1929	Certified Correct
Nebraska	36		F R LOVELAND,
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# BLOOD CHEMISTRY

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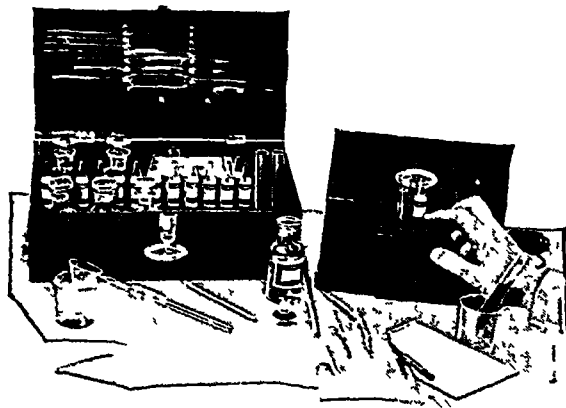
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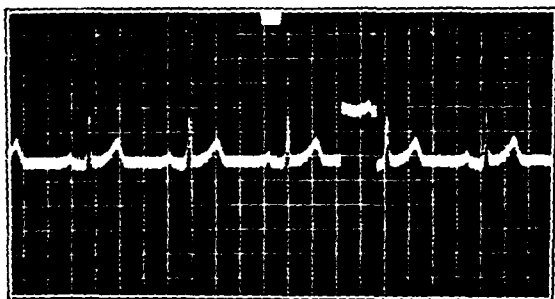
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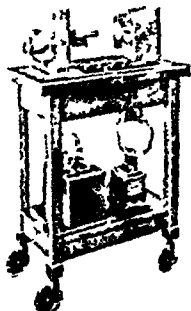
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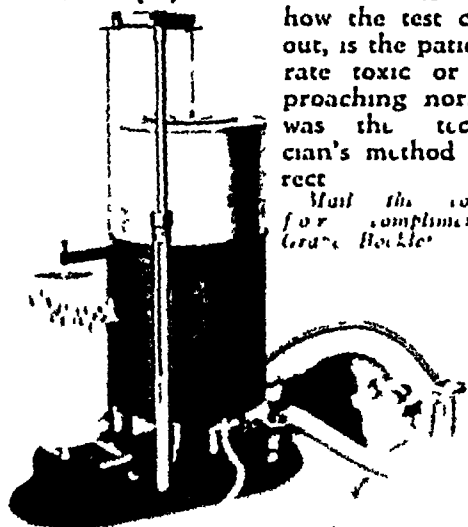
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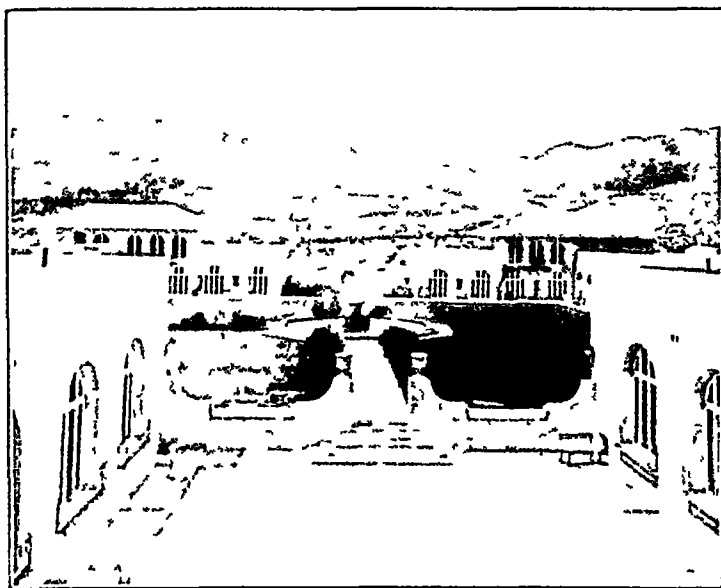
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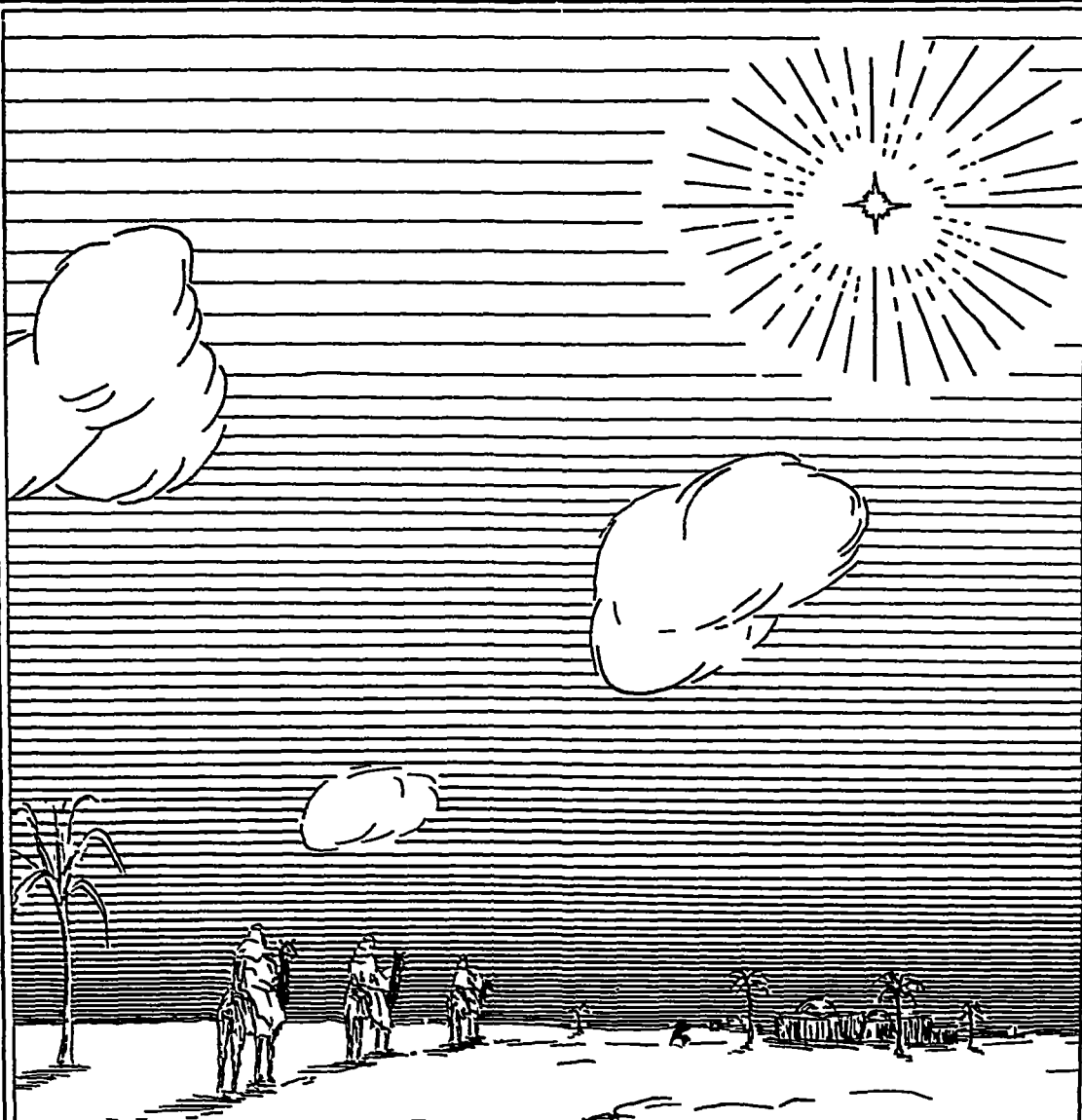
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This manual is a practical guide to the care of the newborn infant. It covers the entire field of obstetrical pediatrics, from the prenatal period to the first year of life. It is written in a clear, concise, and practical manner, and is illustrated with numerous photographs and diagrams. It is a valuable reference work for all who are concerned with the care of the newborn infant.

LEA & FEBIGER

Philadelphia

# Mucous Colitis\*

## Observations in 500 Cases,

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**M**UCOUS COLITIS may be characterized as an affection in which more or less mucus is discharged from the bowel usually associated with colic and in which functional nervous manifestations are prominent

The first allusion to colitis is noted in Chronicles II, Chapter 21, verses 12-19 "Thou shalt have great sickness by disease of thy bowels until thy bowels fall out by reason of the sickness day by day" It was first accurately described by Richard Powell in 1818 and in this country by Mason Good<sup>2</sup> (1825) under the name of diarrhea tubularis According to Woodward, however, Fernelius<sup>3</sup> was the first to draw attention to this condition

In modern times, the first accurate accounts of this affection were given by DaCosta<sup>4</sup> in this country and by Von Leyden<sup>5</sup> in Germany which were further followed by an important description by Nothnagel<sup>6</sup> who suggested the term "mucous colic"

**Etiology** Three views as to the nature of this condition have been maintained

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1 That it is purely neurogenic and that the mucus produced is entirely a nervous hypersecretion a conclusion recently again emphasized by Bockus, Bank and Wilkinson<sup>7</sup>

2 That it is catarrhal in nature produced as the result of inflammation of the mucus membrane of the colon

3 That it is in part neurogenic and in part inflammatory

Although there has been much discussion authorities have not agreed definitely regarding the etiology of this affection In a few instances in which autopsy findings have been recorded definite catarrh with increased production of mucus forming cells have been observed while in others no abnormality was discovered Hurst<sup>8</sup> concludes that the constant appearance of epithelial cells in various stages of degeneration with the addition of leucocytes which are frequently noted in mucous colitis is evidence sufficient to indicate the presence of a definite inflammatory affection

Certain authorities as Nothnagel<sup>6</sup> in order to harmonize these conflicting views contend that there may be two varieties of this condition one a mucous colitis of nervous origin and the other of inflammatory nature However, as Hurst<sup>8</sup> points out these are probably varieties of the same condition bearing somewhat the same rela-

tion as is observed in asthma as compared with bronchitis

From a study of our cases together with a rather careful review of the extensive literature of this subject, we feel justified in drawing the conclusion, that mucous colitis is purely of neurogenic origin and that the discharged mucus can be considered entirely in the light of a nervous hypersecretion. This stage may continue on with exacerbations and remissions for a considerable period of time associated with spasticity of the colon from which recovery may occur, or in some instances, due to a lowered resistance of the bowel, infection may take place with the production of inflammatory changes of a more or less intense type which may finally eventuate in the production of an ulcerative colitis. A number of instances in which these changes have occurred have been ob-

changes in the nervous system have usually existed prior to the development of the intestinal affection. Bockus, Bank and Wilkinson<sup>7</sup> conclude that the etiology of mucous colitis is closely associated with alteration of function of the vegetative nervous system.

While there can be no question, therefore, that there are a number of factors entering into the etiology of mucous colitis, this condition manifests itself mainly in individuals prepared by an instability of the nervous system. The vegetative nervous system supplies two sets of nerve fibres to the gastro-intestinal tract, the one functioning as activator and the other as inhibitor nerves, the two combined exhibiting a regulating mechanism controlling the interactivity of both groups. In the first set we have the parasympathetic system, the stimulation of which results in the production of increased secretory and motor ac-



Shows a string sign in a small portion of the lower bowel

dition the secretory fibres are involved mucous colitis is produced. In the study of this disorder, it becomes evident that the instability and abnormal irritability of the nervous system is a factor of considerable importance in its etiology and most authorities contend that the nervous element (vagotonia), as commonly observed in neurasthenics, the hysterical and hypochondriacs, plays an important rôle in this respect. However, according to Bockus<sup>7</sup> and his collaborators there is often evidence not only of vagotonia but also of sympathicotonia.

The constitutional factor from an etiological standpoint has not been sufficiently emphasized. There is sufficient evidence in many instances to indicate a correlation between physical type in the form of the asthenic indi-

Bockus on the other hand considers this condition a result rather than a cause of the mucous colitis. Constipation existed in 360 of our cases (72 per cent).

(2) Visceroptosis. Attention has already been directed to the occurrence of mucous colitis as a constitutional defect. There is little question, but that this element plays an important role in the etiology of mucous colitis in hypothermic individuals affected with visceroptosis. Enteroptosis occurred in 293 of our cases (58 per cent). In this series 64 per cent of the cases were of the asthenic type and 10 per cent hyperthermic.

(3) Chronic Diseases of the Gall Bladder and Appendix. Gall bladder affections are frequently associated with mucous colitis. At times the dis-

dysmenorrhea and pelvic inflammatory conditions are commonly associated with mucous colitis. The intestinal affection frequently becomes aggravated when exacerbations of the pelvic disorder occur. Menstruation at times causes an increase in the symptoms in patients affected with mucous colitis, a condition which also occurs not infrequently at the menopause. Pelvic disease was noted in 76 of our cases (15 per cent).

(5) Endocrine disturbances. Colitis is often associated with abnormal endocrine function. Of these thyroid and suprarenal dysfunction are most frequent. Both hyper- and hypothyroid states are observed in this condition. Hyperthyroidism was noted in 29 of our cases (5 per cent) and hypothyroidism in 15 (3 per cent).

(6) Food Allergy. Vaughan<sup>10</sup> in 1922 first recorded a possible allergic factor in the causation of mucous colitis and Duke<sup>11</sup> and Andresen<sup>12</sup> described instances in which food allergy caused gastrointestinal colic, Holland<sup>13</sup> and more recently again, Vaughan<sup>14</sup> have reported cases of mucous colitis due to food hypersensitiveness. This condition was noted in 9 of our cases (1 per cent).

(7) Abdominal Adhesions. Pericolitis due to adhesions involving the colon is frequently a causative factor in the production of this disease. Adhesions often arise following abdominal operations and were present in 185 of our cases (37 per cent).

(8) Gastric Dyspepsia. It is not unusual to observe in patients affected with mucous colitis pronounced forms of gastric dyspepsia. As a constitutional defect gastroparesis is not un-

common, and in consequence gaseous distention, eructations following meals, pain, nausea and vomiting may occur. Tachycardia is not uncommon. In some instances the stomach may itself present no abnormalities, and yet the gastric symptoms occur associated with meals, which may be accounted for by the well known gastro-colic reflex. Gastric symptoms were present in 321 of our cases (64 per cent).

(9) Intestinal Dyspepsia and Stasis. The dyspepsia may be either of the fermentative or putrefactive type and under either condition may finally terminate in a mucous colitis. Intestinal stasis also plays an important rôle in the etiology of this affection. The stagnation in the bowel may lead to the development of high degrees of putrefaction with infection of the mucosa, and finally be followed by a mucous colitis. In our series intestinal stasis with dyspepsia was observed in 136 instances (27 per cent). Inasmuch as intestinal stasis is so frequently associated with mucous colitis a subsequent toxemia not uncommonly results.

Occasionally as has already been pointed out in certain instances of mucous colitis of long standing severe infection may follow with the production of more or less serious types of ulcerative colitis. In these cases the stool becomes more or less diarrheic, contains mucus, blood and pus, is extremely fermented and offensive and fever may develop. It is in these instances that either bacteria of the proteolytic (colon group) or of the saccharo-butyric type are found predominant in the stool.

(10) Focal infections. Mucous co-



Shows a long string sign involving the entire lower colon

litis may undoubtedly develop in some instances as a result of focal lesions in the teeth, tonsils, sinuses or gall bladder. There was direct evidence of focal infection in 118 of our cases (23 per cent).

It is not uncommon according to our experience that a number of the factors above noted may act together as causative agents in the production of mucous colitis.

**Incidence** Mucous colitis occurs most frequently in the female sex. It has been estimated that the usual proportion of females to males affected is as five to one. The disease is most common in middle life and especially noted between the 20th and 40th years. It occurs however in old age and cases have been recorded in children. In our series of 500 cases there were 424 females and 76 males, a proportion of about  $5\frac{1}{2}$  females to 1 male.

The following presents these cases arranged according to age and sex.

Ages	Females	Males
10 to 20	18	5
20 to 30	101	16
30 to 40	114	19
40 to 50	88	21
50 to 60	84	10
60 to 70	19	5
Total	424 (84%)	76 (15%)

**Pathology** Although there has been much discussion, there still remains a considerable difference of opinion regarding the pathological changes occurring in the bowel in mucous colitis. Opportunities of performing autopsies upon patients affected with this condition have been rare so that but little is known of the actual pathology of

this affection. In certain specimens of colons removed at operation the mucosa has been found normal, but the mucous glands and follicles are usually observed distended with mucus, congested and inflammatory changes are noted. The discharge of mucus in the form of membrane frequently contains epithelial cells in large numbers in various stages of degeneration, indicating an unquestionable profuse desquamation from the mucous membrane of the bowel, and when, as Hurst<sup>8</sup> points out, leucocytes are also present additional evidence is afforded to indicate the inflammatory nature of the process. It is interesting to note, as Bastedo<sup>15</sup> has recently pointed out, and which is in accord with our experimental observations, that the disease is not limited entirely to the colon but also at times invades the lower ileum.

Norman and Eggston<sup>16</sup> group the intestinal toxemias occurring in advanced forms of mucous colitis into two types.

- (1) Putrefactive toxemia
  - (a) Indolic type with indicanuria
  - (b) Indolic type without indicanuria
  - (c) Butyric acid types
- (2) Pyogenic infective toxemia associated with focal infection of the bowel

According to these observers, the pathological changes noted in intestinal stasis with mucous colitis are hyperplasia of the intestinal chain of lymphatics, diffuse infiltration of the intestinal mucosa with lymphocytes, eosinophiles, plasma cells, and in some instances areas of polymorphonuclear



infiltration forming small abscesses. In the more chronic cases, the submucosa is fibrous and reveals hyperplastic lymph follicles and diffuse infiltration of mononuclear cells. The muscular coat becomes next invaded and presents inflammatory infiltration with fibrosis and a partial destruction of smooth musculature. In consequence of the fibrosis a loss of elasticity of the wall of the bowel is produced, resulting in intermittent dilatation of the intestines and finally chronic dilatation with thinning of the colonic wall.

Microorganisms of many forms have been observed in the stools in cases of mucous colitis, but none of etiological importance has been determined.

**Symptomatology** The most common symptoms are chronic constipation associated with colicky pain and the passage of mucus. Colicky pain may however be absent and is frequently replaced by simple abdominal discomfort. Many of these patients present a history of long standing and increasing constipation often dating back to childhood and not uncommonly associated with neurasthenic symptoms.

Previous to the first attack premonitory dyspeptic symptoms consisting of pressure, fulness, distention, flatulency and abdominal discomfort often occurs. At this period, the passage of small bits of mucus are not infrequently noted mainly surrounding the hard fecal masses. The first attack is usually ushered in suddenly with or without apparent cause with intense colicky pain followed by the passage of mucus. The immediate cause of the attack is often attributed to an

increasing constipation, to nervous excitement, fatigue, menstrual disturbances or even errors in diet. The mucus is discharged in large amounts in a single evacuation or in small quantities at short intervals. Its passage is usually followed by relief from pain. The mucus frequently surrounds small scybala or is discharged with the feces or alone. In some instances, even of a severe type the passage of the membrane occurs without pain. This is however unusual though it occurred in a number of instances in our series. Not infrequently, however, following severe attacks of colic, mild forms are apt to occur also followed by a mucous discharge.

In the intervals between the attacks the patient is frequently in comfort, though in many instances dyspeptic symptoms with dull abdominal pain occur, not uncommonly associated with psychoneurotic manifestations and persistent lassitude. The duration of the interval between attacks is variable. In some instances a few days may elapse between attacks while in others there may be weeks, or even months.

The attack itself is ordinarily of several hours duration from the time of the onset of the colic to the final completion of the mucus discharge, though in some instances it may extend with minor remissions over a period of days. It is frequently accompanied by nausea, vomiting, weakness and occasionally with signs of shock. Occasionally mucus is vomited at this stage, and a rise in temperature may occur. The pain is most commonly noted in the left lower abdomen and



Same case, illustrates the absence of haustra, following a colon enema

there is usually tenderness in this region as well as along the course of the descending colon. The pain is not infrequently relieved by a movement of the bowels. Contracted painful areas can at times be palpated in the region of the descending colon and sigmoid, indicating a spasticity of the bowel. Similar manifestations are less frequently observed in the region of the cecum ascending and transverse colon, and may lead to an erroneous diagnosis of appendicitis, cholecystitis or diverticulitis.

Patients affected with mucous colitis as has already been noted usually suffer with chronic constipation of so severe a type that the most drastic remedies are often required to secure proper bowel evacuations.

According to Von Noorden<sup>17</sup> constipation which is of the spastic type, occurs in at least 80 per cent of the cases. At times the constipation may be followed by diarrhea which may continue for a period of days. This is produced by the irritation of the feces retained over days inducing an actual colitis which however may again disappear after a short interval or continue on to produce a definite chronic colitis. In fact, Mallory<sup>18</sup> maintains that ulcerative colitis is but the final stage of mucous colitis. In a small proportion of cases constipation is entirely absent, the discharges being normal in consistency or even soft. This has been estimated to occur in about 20 per cent of cases. In these cases there is present in addition to the excess of mucus in the stools, evidences of fermentation indicated by the presence of gas bubbles and an extremely fetid acid odor together with

a resultant putrefactive and pyogenic infective toxemia. Occasionally blood is found in the stools in mucous colitis though this is rather rare.

Boas<sup>19</sup> has recently called attention to a symptom observed at times in mucous colitis which he terms *pyrosis coli*—a burning pain along the course of the colon, and associated with the chronic constipation and discharge of mucus. This condition is independent of the ingestion of food, and is probably due to excessive fermentation in the bowel. In our series typical attacks of *mucos colic* were observed in 250 instances (50 per cent); in 185 (37 per cent) there was more or less generalized abdominal pain and discomfort, and in 39 (7 per cent) pain was entirely absent although indigestion and abdominal discomfort was noted. It was more particularly localized in the lower left quadrant in 91 instances (18 per cent), in the upper abdomen in 38 (7 per cent); in the lower right quadrant in 12 (3 per cent), in the upper right quadrant in 23 (4 per cent), in the upper left quadrant in 32 (6 per cent), in the umbilical region in 38 (7 per cent) and in the lumbar region in 11 (2 per cent). In 52 (10 per cent) it was variable in location. Tenderness on pressure was noted over the entire colon in 213 instances (42 per cent), it was almost entirely limited to the lower descending colon in 96 (13 per cent) to the ascending colon in 28 (5 per cent) and to the transverse colon in 9 (1 per cent).

Chronic constipation existed in 360 of our cases (72 per cent), alternating constipation and diarrhea occurred in 54 (10 per cent), diarrhea in 45 in-

stances (9 per cent), normal bowel movements were noted in 10 instances (2 per cent)

**The Mucus** The glands of the colon secrete the mucus which is converted into shreds, compact masses and membranes and at times soft gelatinous material. The appearance often indicates that the passage of these membranes is not immediate following excretion, but the mucus evidently remains in the haustra of the colon for some time being moulded into various shapes by pressure from the hard fecal masses. The membranes are at times easily recognizable casts of secretions of the colon with the location of the follicles quite evident. They are transparent or opaque usually white in color but may be brown stained by the feces and occasionally red by blood. The wall of the membrane is laminated and bits of feces can be detected between the laminae. The diameter of the tube may reach one and one-half inches, the wall is usually thin, but may become greatly thickened. The membrane may be discharged as a solid ball alone or together with fecal masses and occasionally these masses may contain the mucus imbedded within or they may be surrounded by this secretion. As has already been noted the mucus is occasionally blood stained due to slight rupture of small vessels in the mucus membrane caused by the passage of hard fecal masses. Chemically the membrane consists mainly of coagulated mucin and not of fibrin as was formerly maintained. Microscopically, the membrane is found to be structureless and transparent and contains within bits of fecal matter, and un-

digested food fibres but is free from signs of inflammation. Only in advanced cases do we find fibrin, leucocytes, epithelial cells, many disintegrated micro-organisms, cholesterol crystals, and phosphates. Under higher magnification the inner surface of the membrane presents a reticulated appearance.

**Intestinal Sand** The passage of intestinal sand is not of uncommon occurrence in mucous colitis, according to Hale White. It may not be observed until late in the course of this affection. It consists of reddish brown or yellow or black sand like granules, discharged in small or large amounts and is composed largely of the calcium soaps of palmitic and stearic acid and calcium phosphate in addition to urobilin and is probably formed in the colon. Intestinal sand observed in mucous colitis must not be confused with false sand produced by the ingestion of large amounts of bananas and pears.

The gastric contents reveals on examination a varied chemistry—achylia and hypochlorhydria are frequent findings though normal acidity and hyperchlorhydria are not uncommon. According to Von Noorden<sup>9</sup> of 20 cases examined 4 showed an achylia, in the others hyperacidity and sometimes subacidity was noted.

The gastric secretion was examined in 411 of our 500 cases. Normal acidity was found in 165 (40 per cent), hyperchlorhydria in 113 (27 per cent) and hypochlorhydria and achylia in 133 (32 per cent).

**Symptoms and Signs of Minor Importance** Bockus, Bank and Wilkinson<sup>7</sup> have carefully studied their cases



String sign in lower bowel, involving the splenic third of the transverse colon. Note the spastic appendix.

of mucous colitis with reference to imbalance of the vegetative nervous system and concluded that in a larger proportion of instances there is an over excitability of both the parasympathetic and sympathetic systems, the former being most marked. In 32 of our cases in which basal metabolism observations were recorded normal findings were obtained in 19, decreased metabolic rate in 6 and increased in 7. These findings correspond closely with those of Bockus who likewise points to the absence of a generally decreased basal rate in his cases.

Of 310 of our cases in which blood pressure readings were recorded hypertension occurred in 32 per cent, hypotension in 39 per cent and normal tension in 29, figures which are also closely in accord with those of Bockus and his coworkers.

Such manifestations as sweating, chilly sensations, tremors, palpitation, urticaria, angio-neurotic edema, dermographism and migrainous attacks, as are noted by Bockus, were also prominent in many of our cases.

**Diagnosis** Inasmuch as our methods of diagnosis have been much improved during recent years many cases of mucous colitis are now recognized which formerly escaped detection. In typical instances the diagnosis is unmistakable. The sudden onset of recurrent attacks of abdominal colic followed by the passage of membranes in individuals affected with chronic constipation renders the diagnosis simple. In those instances however in which the symptoms are atypical, there may be considerable difficulty in arriving at a correct conclusion.

This may occur especially during the first attack in which the pain may precede the discharge of mucus by a considerable length of time. On the other hand, however, attacks of mucous colitis may appear as apparently typical but may be caused by diseases of other organs and the underlying condition may be entirely overlooked. The attacks of pain may especially simulate such affections as renal colic, appendicular colic, biliary colic or the pain produced by a twisted ovarian cyst. A thorough examination, to which reference will be called later, will however usually lead to the correct diagnosis. It is interesting to note, that 82 of our cases had been subjected to abdominal operations. Of these 24 (28 per cent) received no apparent relief from the procedure. The operation consisted of appendectomies, cholecystostomies, cholecystectomies, release of adhesions and pelvic operations. The absence of the admixture of mucus with the stool does not necessarily indicate according to Strauss<sup>20</sup> the non-existence of a mucous colitis. In doubtful cases cleansing injections may be employed in order to demonstrate its presence.

Additional aid in diagnosis is obtained by means of sigmoidoscopic examinations, through which important information may be obtained. In the early stage of this affection the vessels of the bowel are greatly engorged, and the capillary injection is especially prominent, the mucus membrane being covered with a glairy mucus which gives an appearance similar to that of shad roe.

In the second stage in which the condition is more fully developed the

appearance is somewhat altered. There is no longer the intense engorgement of the membrane, nor do the vessels stand out prominently, neither the intense glary appearance of the membrane, nor the marked increase of mucus covering the entire mucous membrane are observed; but distinct areas in which the mucous membrane is covered with a thick tenacious mucus which adheres closely and which at times can only be removed with difficulty. This condition gradually passes into the third stage in which the mucous membrane seems to be thinned out, pale, covered with mucus, and at times membranes are noted. When these membranes are removed small pin-head ulcerations are observed. These are not typical ulcerations but appear as though the mucus membrane is slightly denuded of its superficial surface. Following the removal of the membrane the mucosa gradually within a few days assumes a nearly normal appearance. Not uncommonly at this stage the mucosa may be observed covered in areas varying from three to four inches with membrane, in other areas with a tenacious mucus. It is an interesting fact that following removal of the mucus by washing with a solution of bicarbonate of soda that the mucosa appears almost normal. Remissions are not uncommon and last for a varying period of time during which the bowels assumes a perfectly normal appearance. If the disturbance progresses however, the mucous membrane may lose some of its resistance and we have noted after a long period of time in a number of instances actual ulcer-

ations occurring as a final process with atrophic changes in the mucosa.

Spasm is not uncommonly noted in the bowel, occasionally to so marked a degree as to make the examination not only difficult but also extremely painful. The sigmoidoscopic examination is not only valuable as an aid in arriving at a diagnosis of this affection but is likewise extremely helpful in excluding associated conditions such as carcinoma. Sigmoidoscopic examinations were made in 438 of our cases and in these definite evidence of mucous colitis was present in 89 per cent.

The roentgen-ray furnishes important information in the diagnosis of mucous colitis and in obscure forms is often invaluable. The technic is followed as in the usual routine gastrointestinal examination. Mucous colitis is best revealed from the twelfth to the twenty-fourth hour examination. The patient is required to return the morning following the administration of the barium meal and after a bowel movement if possible. Not infrequently following an action the roentgen signs are observed to the best advantage. If no bowel movement occurs only a very small area of the bowel may present the so-called "string sign" or there may be only spasm at hand with marked increase of the haustra. At times no roentgen evidence whatever will be noted in the examination. Spasm of the bowel is an early roentgen finding of this affection but occurs in so many other conditions that its significance is much lessened. At times a feathery appearance of the bowel is observed, most frequently noted in the descending colon. The



An unusual long string sign, involving almost the entire colon



feathering of the colon simulates the appearance of the small bowel. The typical "string sign" which may be revealed at any stage is an extremely characteristic sign of mucous colitis. The fluoroscopic examination during the eighteen hour period does not always reveal these changes due to the small amount of the opaque meal in the bowel. At times the "string sign" is so thin and faint that it can only be determined on a well taken film. This occurs so frequently according to our experience, that we no longer rely on the fluoroscopic examination.

The "string sign" of mucous colitis is by no means always a constant finding. It may be observed at any portion of the colon, the most frequent site being in the descending colon, the transverse colon to a lesser degree. The ascending colon and cecum may also present this sign in rare instances. The calibre of the string line varies usually from one half to two mm in diameter but may be larger in some instances. The line is usually straight and continuous, and as a rule presents no break in its full length. Very frequently the "string sign" begins with the feathery appearance for several inches and then tapers off into the string. According to Crane<sup>21</sup> the "string sign" is produced through the spasticity of the bowel undergoing certain peristaltic movements upon the mucoid material. It occurred in 10 per cent of our cases.

The routine barium colon enema does not always present much direct evidence, the meal flows up the colon readily and no abnormality of the lumen is noted under the fluoroscope, while in the film very frequently the

descending colon will reveal an absence of haustra and at times some narrowing which is quite suggestive of a colitis. In our routine enema an immediate film is made of the colon and another film following the elimination of the barium. In the latter examination the string sign or feathery appearance of the colon will often be revealed in cases of mucous colitis. It has been observed according to our experience, even when the routine gastro-intestinal study was negative.

Kantor<sup>22</sup> has advised as a routine that a nine hour observation be made following the administration of the barium meal. At this period hypermotility of the intestinal tract will be noted, the barium appearing in the pelvic colon and rectum. This sign is however variable and may even occur in other conditions. In mucous colitis on the other hand due to the usual constipation as well as the marked spasticity of the colon, hypermotility is often not present. No abnormal roentgen changes were revealed in the cecum or ascending colon in our series. The ileum presented no eighteen hour residue or other abnormal changes. In addition the X-ray revealed ptosis of the colon in 58 per cent and spasm in 51 per cent of our cases. It further presented evidence of gastric ulcers in 3 per cent, of duodenal ulcer in 5 per cent, of chronic cholecystitis in 18 per cent of which 4 per cent were cases of cholelithiasis, of duodenal dilatation in 1 per cent, of chronic appendicitis in 24 per cent, and of diverticulitis in 1 per cent.

**Differential Diagnosis** It is important to distinguish between the true forms of mucous colitis, and those

produced as secondary manifestations of other diseases of the bowel. Mucus in the form of membranes may be discharged for example in such conditions as cancer and ulcerative colitis.

On the other hand mucous colitis may simulate cholecystitis, appendicitis, peptic ulcer, intestinal polyps, carcinoma, diverticulitis, ulcerative colitis, renal colic and ovarian cyst with twisted pedicle.

When the hepatic flexure is mainly involved, the affection may suggest cholecystitis, when in the cecal region, appendicitis may be simulated and when in the transverse colon peptic ulcer. A careful physical as well as X-ray and proctoscopic examination will ordinarily lead to a correct diagnosis and prevent the serious error of advising unnecessary surgical interference.

Polyps, carcinoma of the bowel and diverticulitis can also be excluded by careful sigmoidoscopic and X-ray investigations. The differential diagnosis between mucous and ulcerative colitis is not always simple, especially when the ulcerations are of a mild type. A proctoscopic examination together with the examination of the mucus discharged is of the greatest importance in diagnosis. In the ulcerative forms there is a constant admixture with pus and frequently blood while in mucous colitis the mucus is free of blood and pus. When the ascending colon is mainly involved severe types of mucous colitis may simulate kidney colic. Here too, a careful examination of the urine, an X-ray of the kidneys and cystoscopic investigation on the one hand, and an examination of the stool, sigmoidoscopic as

well as an X-ray investigation following a barium meal on the other, will usually lead to a correct conclusion. An ovarian cyst with twisted pedicle can usually be excluded by means of a careful pelvic examination.

**Prognosis** The prognosis for complete recovery in mucous colitis depends largely upon the duration of the disease which may in some instances extend over many years. In early cases if treatment is promptly and carefully instituted recovery is to be expected. Of this type, Schmidt-Von Noorden<sup>17</sup> contend 90 per cent should entirely recover. In late cases however, and especially those in which secondary changes have occurred, the prognosis must be guarded. However, even in these, abdominal colic and discomfort may often be overcome and the patient be entirely relieved of annoying symptoms.

Relapses are common in all forms. According to Von Noorden<sup>17</sup> the prognosis is far less favorable in those instances not associated with constipation and relapses are here far more common.

According to the statistics of Von Noorden<sup>9</sup> of 76 cases treated complete success of treatment occurred in 79 per cent, incomplete success in 15.8 per cent, permanent success in 50 per cent, relapses in 13.1 per cent, unknown 15.8 per cent, failure in 5.2 per cent.

**Treatment** In the treatment of mucous colitis it is obvious that the cause must as far as possible be first overcome. On this account, it is of the utmost importance, that a general as well as complete survey of the patient be undertaken. Focal infections of

whatever nature must be eradicated. The entire gastro-intestinal tract must especially be examined in order that any possible causative factor may be discovered and corrected.

If the theory be accepted, that mucous colitis has its origin in an imbalance of the vegetative nervous system and is therefore a purely functional affection, the method of treatment becomes evident. Inasmuch as the disease is observed in psychoneurotics, a careful analysis into the patient's emotions and mental state must be undertaken. Reeducation is essential in the cure of these invalids, and every effort should be made to alter the patient's attitude toward existing conditions. This is not always a simple matter, and not infrequently many prolonged consultations must be held before the patient's confidence is restored, and an insight gained in, to the true state of his condition. Unless he realizes, that his disability is purely functional and remediable largely through his own efforts but slight relief can be expected.

The constitutional factor must also be taken into consideration. The exhaustion of the nervous system which is the cause of the physical and mental fatigue still further depresses the already weakened constitutional defect. Consequently it is of the utmost importance for individuals affected with mucous colitis that overwork be avoided, and that a requisite amount of rest as well as diversion be obtained.

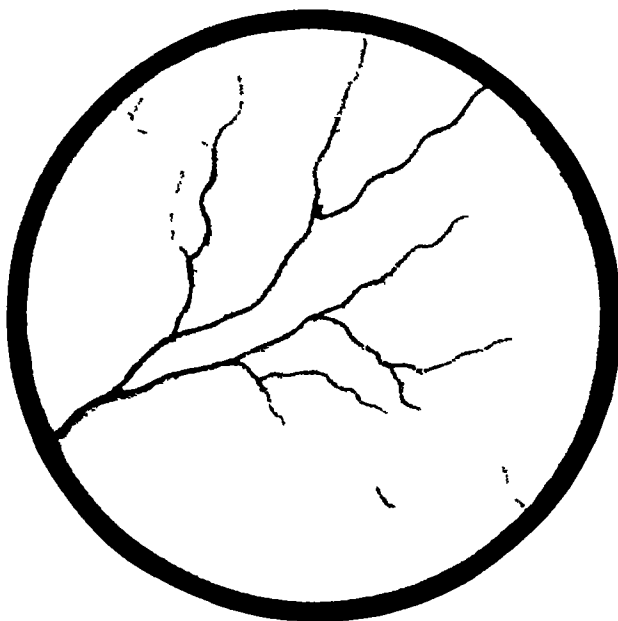
The regulation of the diet plays an important rôle in the treatment of mucous colitis. However, authorities have not been in accord regarding the character of the diet to be prescribed.

Some as Von Noorden<sup>8</sup> advocate the employment of a diet containing large proportions of an indigestible residue with an excess of fat. According to this authority a cure can be more easily effected by rapidly overcoming the constipation brought about by this method of treatment. The food should consist mainly of bread containing an excess husks (graham bread), in addition to vegetables containing much roughage and fruit with seeds. As an essential feature of this method, Von Noorden advises that the change from a bland to this indigestible laxative diet should be brought about suddenly and not gradually, even though the symptoms become at first aggravated. As a result of a diet of this type the formation of hard stools is prevented and they become soft and abundant. The favorable effect of a diet of this type is attributed mainly to the large amounts of cellulose which it contains.

According to other authorities as Fleiner<sup>23</sup> and Schmidt<sup>21</sup> the diet should be so regulated as to protect and spare the bowel undue irritation as far as possible, and they therefore advocate the use of a bland non-stimulating diet producing but a small residue in the bowel. In order to overcome the tendency to the formation of extremely constipated stools Fleiner advises the systematic employment of retention oil enemata.

According to our experience any strict inelastic diet should not be prescribed. Under all conditions a rational diet based largely upon the needs of the individual is to be advised.

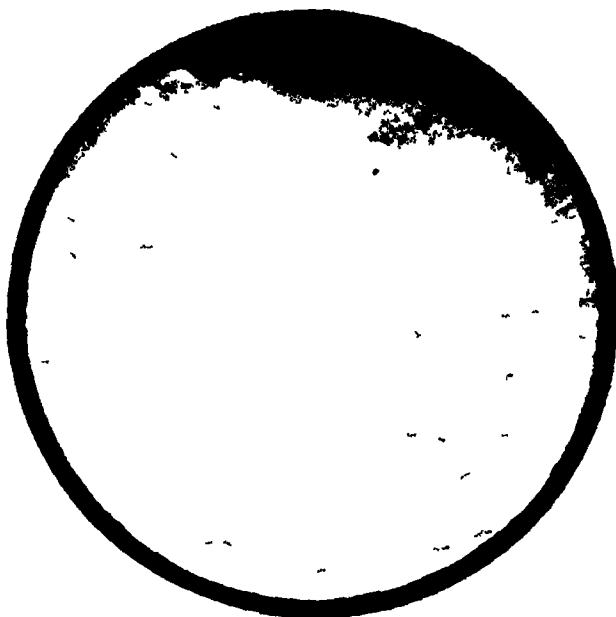
In general it is best at first to place the patient upon bland food, and grad-



Shows dilatation of the capularies in the first stage



Illustrates the first stage, showing the shadroe variety of mucous colitis, with acute manifestations



Shadroe variety of mucous colitis, the appearance of the mucous membrane, overshadowed by mucus



Illustrates the second stage, showing a plastic proctitis, with intense engorgement of the mucous membrane



Shows the combination of the first and second stages



Membranous or third stage, membrane rolled over to show the inflammatory condition of the bowel

usually increase to a nutritious mixed and laxative diet, which should not be however too coarse. On a diet of this type the movements of the bowel usually become more normal and the secretion of mucus lessened. In the milder cases, a diet consisting largely of roughage may be prescribed at times at the onset with advantage.

In addition the food should be regulated with a view of overcoming certain underlying causes as well as contributing factors such as anemia, undernutrition and various digestive disturbances which may be at hand. In some instances the "smooth diet" of Alvarez<sup>27</sup> may be followed with advantage for a time.

The special management of a number of associated conditions require further consideration, of these colic, constipation and undernutrition are most important. With the onset of colic the pain may be so intense as to require immediate bed rest. Under all circumstances, it is important whenever the colic is frequent or is intense, that the patient be at rest until this symptom abates. The application of hot stupes to the abdomen usually affords considerable relief. In extreme cases, codeine, pantapone or even morphia may become necessary. At times benefit may be obtained from the administration of atropine hypodermically. In milder cases relief is often afforded by the use of enemata of hot water or of oil retained over night. In the early stages, the use of purgatives must be avoided.

The diet should be of the liquid and soft variety at this period and atropine or belladonna should be administered in adequate doses. In some in-

stances in our experience great benefit is derived from luminal given in moderate doses ( $\frac{1}{4}$  grain) three or four times daily. The proper management of the chronic constipation so constantly present in mucous colitis is of extreme importance. Attention has already been directed to the dietetic measures so essential in the treatment of this symptom. In addition the use of acidophilus milk to which milk sugar may be added has been found useful. Cohnheim<sup>28</sup> has recently recommended the employment of bitter chocolate bars. Three to four ounces are to be consumed daily for this purpose. The patient is ordered one ounce in the morning before breakfast, and a similar amount at bedtime, to be followed by 3 to 4 ounces of water. In addition three quarters of an ounce is to be taken before luncheon and before dinner. In some instances one or two ounces per day is all that may be required for this purpose, in others five ounces may become necessary.

The oil enemata which are to be retained over night are extremely useful in regulating the bowel movements, in some instances the employment of saline or bicarbonate of soda enemata become essential. The indiscriminate use of purgatives is to be avoided. Castor oil is valuable at times, when administered at weekly intervals in doses of one half to one ounce or small doses may be prescribed to advantage given in capsules three or four times daily. Mineral oil and agar-agar are useful in some instances in regulating the bowels and olive oil taken in adequate amounts is invaluable for this purpose especially when

malnutrition exists. Not infrequently great relief may be obtained by a sojourn at mineral spas at which the water is recognized to possess a remedial effect in this affection. Of these Bedford, Saratoga and White Sulphur are useful examples in this country and Kissingen, Carlsbad, Marienbad, Vichy and Neuenahr in Europe. It is a well observed fact, that the cure of the constipation is likewise frequently followed by a cure of the colitis, which according to Schmidt and Von Noorden<sup>17</sup> indicates that the irritation of hard scybalous masses may have some bearing in the etiology of mucous colitis. On the other hand relief in this disease is by no means always noted by a cure of the constipation, and in many instances even when this symptom is effectively overcome, large quantities of mucus still continue to be discharged. Overcoming undernutrition is important in the relief and cure of this disease. In the aggravated types, in which there is marked loss of flesh and which are frequently complicated with marked grades of enteroptosis, well planned rest cures become essential. These should be directed not only toward building up of the physical condition of the patient by a gain in weight and improvement in the blood picture, but also in improving the state of the nervous system by means of psychotherapeutic measures. An increase in flesh and improvement in the general nutrition will also often markedly overcome long standing and severe types of mucous colitis and thus relieve the patient of depression and nervous fears. This treatment is best undertaken in a hospital or sanatorium,

and should extend over a period of from four to eight weeks. Additional benefit may be obtained during this period from the judicious employment of hydrotherapy, heliotherapy, diathermy as well as from application of medicated stupes to the abdomen. In the enteroptotic patient the application of a well fitting abdominal support following the bed rest is of distinct advantage. In certain instances in which a gain in weight cannot be accomplished through forced feeding, this may be brought about as Frank<sup>27</sup> has recently pointed out, by the administration of insulin with the addition of adequate amounts of carbohydrates. Colonic irrigations with medicated solutions so commonly practiced in this condition are of extremely doubtful utility. The irritation of the bowel is apt to be increased by such measures and they are likewise harmful in further undermining the nervous system in these psychoneurotic individuals by centering the patients attention too closely upon his disability. Water or a weak solution of bicarbonate of soda in the form of irrigations may be helpful when employed once or twice weekly in some instances. In others great relief may be obtained from the instillation and retention of olive oil in the bowel over night, or of two ounces of a two to four per cent solution of protaigol, or a five per cent gelatin solution, as has been recommended by Dudley Roberts.

Drugs play but a very unimportant rôle in the treatment of mucous colitis. Intestinal antiseptics are useless. Attention has already been directed to the value of castor oil as well as mineral oil for the relief of constipation.



Drastic purgatives should never be employed

There are few other drugs of value in this affection. Atropin and belladonna in increasing doses are especially helpful in overcoming spasm. Such sedatives as valerian, the bromides and luminal are at times, exceedingly useful. Whenever there is an absence of hydrochloric acid or a diminution of this acid in the gastric secretion mucinatic acid is indicated, while if hyperacidity is present alkalis should be administered. According to Bockus, Bank and Wilkinson, the use of calcium combined with parathyroid gland may be helpful in the treatment of this condition. Such surgical procedures as appendicostomy or caecostomy, which have been advised from time to time for the treatment of this affection are unnecessary and cannot be too strongly condemned.

#### SUMMARY

Three views as to the nature of mucous colitis have been maintained. 1. That it is purely neurogenic and that the mucus produced is entirely a nervous hypersecretion, 2. that it is catarrhal in nature produced as the result of inflammation of the mucous membrane of the colon, 3. that it is partly neurogenic and partly inflammatory. The impression is gaining ground that in most instances at least there are inflammatory changes at hand even though these be of a mild type. There is no question, however, that this condition manifests itself mainly in individuals prepared by an instability of the nervous system. There is also sufficient evidence to indicate that this constitutional factor plays an important etiological rôle and that there is

a correlation between the physical type and the secretory and motor disturbance.

As contributory factors associated with the development of this affection are chronic constipation, visceroptosis, cholecystitis, appendicitis, chronic disease of the female generative organs, endocrine disturbances, food allergy, abdominal adhesions, gastric and intestinal dyspepsia and focal infections.

Mucous colitis occurs most frequently in the female sex and is most common between the twentieth and fiftieth years. The usual symptom is chronic constipation associated with colicky pain and the passage of mucus in the form of membranes. The gastric contents reveals a varied chemistry, achylia and hypochlorhydria being most common. In typical instances the diagnosis is simple. Attacks of mucous colitis may, however, simulate other affections or may be secondary to other more serious disorders. Sigmoidoscopic and roentgen ray examinations are important as methods of diagnosis. The roentgen "string sign" is especially valuable in this regard though it is not constantly present.

In the treatment, it is important that the causative factors must as far as possible be overcome. Focal infections must be eradicated. The nervous system especially requires careful supervision. The diet must be carefully regulated though a strict inelastic diet should not be prescribed. A rational diet based largely on the needs of the patient is to be advised, which should be regulated to overcome the constipation, undernutrition and the various digestive disturbances which may be at hand. Colonic irrigations

are of doubtful utility and drugs play an unimportant rôle Atropin or belladonna are of value in overcoming spasm Surgical procedures are unnecessary and should not be undertaken

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# The Principles Under-Lying the Calculation of Flexible Diabetic and Ketogenic Diets\*

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**T**HERE is a constant pressing demand by medical students, hospital internes and practitioners, who have not had a large experience in quantitative diet adjustment, for a simple and direct method of calculating diets. To be valuable, such a method must be adequate to meet the varying clinical situations presented. Many attempts have been made to answer this question. In most of those published, there is either a lack of flexibility, which handicaps one in dealing with the different clinical problems, or else a system of test diets is proposed which is applicable to classes rather than individuals. The present method allows one to calculate with equal ease a diet for a patient with an acidosis or one for a patient with a relatively mild diabetic defect. It treats the patient as an individual and offers a direct method of calculating the diet factors with a minimum of re-adjustment. It has been in use four years at the University of Illinois and has been very helpful in teaching the subject to medical students.

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## THE TOTAL CALORIES IN THE DIET

Following the suggestion of Wilder,<sup>1</sup> an adult at bed rest is given either his basal requirements or basal plus 10%. An ambulatory patient is given basal plus 30%, and a patient at work, basal plus 50% to basal plus 75%.

This method was used by Campbell<sup>2</sup> and Ladd and Palmer,<sup>3</sup> and is now in general use. The nomographic chart of Boothby and Sandiford<sup>4</sup> for estimating the basal requirements, facilitates this calculation.

In the case of children there is less agreement as to the total calories to be fed. This is due to the absence of a definite method of measuring the calories necessary for growth and activity. In the case of infants and children below 7 years of age, confined to bed, Benedict and Talbot<sup>5</sup> estimate that during moderate activity the metabolism is 25% above the basal level. When the child is relatively quiet, the metabolism is 15% above basal. Something must be added for the specific dynamic effect of food, so a safe caloric level at which children below 7 years may be maintained during short periods of desugarization and diet adjustment, is basal plus 30%. After the child passes 7 years of age, Benedict and Talbot estimate that very

little is to be added for activity when the patient is confined to bed. The requirements then for such a child at bed rest, are approximately basal plus an increment for specific dynamic action of food. Hence these children may be safely maintained for short periods at basal plus 10% to basal plus 15%.

Benedict and Talbot have discussed the food requirements for activity. During bed rest and sleep (10 to 12 hours), the requirements are basal; during the time spent in the school room and devoted to moderate activity (6 to 8 hours), they are basal plus 75%; during the period of actual play (4 to 6 hours), there are no measurements available. In many children this requirement may be basal plus 200%; in others much less. Hence the total quantity of food prescribed will have to be determined by studying the child as an individual and by consulting statistical studies of food consumed by healthy growing children. The estimates of Holt and Fales<sup>6</sup> have made liberal allowances for activity based on such studies. By reference to Table II, it will be noted that the calories advocated by Holt and Fales correspond fairly closely to basal plus 100% on the basis of Benedict and Talbot's predictions.

Talbot and associates<sup>7</sup> in discussing the treatment of epileptic children advise the use of diets containing basal plus 50%. Ladd<sup>8</sup> finds that satisfactory growth occurs in diabetic children on diets 40% to 50% below the standards set by Holt and Fales. This corresponds to basal plus 50% to basal plus 60%, on the basis of Talbot's predictions. Bartlett<sup>9</sup> found that his

children showed a positive nitrogen balance when the total calories of the diet approached those advocated by Holt and Fales. G. L. Boyd<sup>10</sup> in summarizing the caloric requirements for growth, considers that the use of Holt's standards are justifiable if the child be fed according to his theoretical rather than his actual weight. Julian D. Boyd and Nelson<sup>11</sup> used Holt and Fales' estimates of energy requirements, and found that their children grew rapidly in height and that they were in advance of the standards commonly used. They contrasted their results with those of Joslin, who fed only  $\frac{1}{2}$  to  $\frac{3}{4}$  of the calories given to their cases. They stressed the value of liberal feeding in stimulating growth in height.

From the above discussion one may conclude that the diabetic child under restricted activity may be fed basal plus 30% for the purpose of desugarization. In view of the insistent teaching that diabetic patients should be kept at a low metabolic level, it would seem wise to feed a diabetic boy, who is being returned to activity, basal plus 75% on the basis of his theoretical weight. Under the same conditions a diabetic girl is to be fed basal plus 50% on the basis of her theoretical weight. Secondary adjustments may then be made as needed to maintain a normal growth curve. The basal requirements are taken from the predictions of Talbot<sup>12</sup> according to height.

#### THE PROTEIN REQUIREMENTS

As a result of the studies of Sherman<sup>13</sup> in the normal subject, and Marsh, Newburgh and Holly<sup>14</sup> in the diabetic, it has been generally accepted

that the adult patient may be maintained in satisfactory nitrogen equilibrium on  $\frac{2}{3}$  of a gm. of protein per kilo body weight. Emphasis also has been laid on the unfavorable effect on the diabetic defect of excessive quantities of protein. It is quite generally agreed that the protein in the adult diabetic diet should range between 0.66 gm and 1.0 gm. per kilo body weight. It is also obvious that, if an adult should be given a ketogenic diet, the protein should be kept low so that the largest amount of carbohydrate may be given.

For the development of the method of diet calculation proposed in this pa-

per, it became necessary to express the calories derived from the protein as a percentage of the total calories. Sherman<sup>13</sup> noted in his experiments that the protein calories necessary for maintenance of nitrogen equilibrium, constitute 6% of the total calories. Du Bois<sup>15</sup> has shown that the normal individual in the post-absorptive state develops approximately 15% of his energy from protein. An intermediate figure of 10% should furnish an adequate but not excessive quantity of protein.

In Table I a study is made of the grams of protein per kilo body weight in the case of men, which are fur-

TABLE I GRAMS PROTEIN PER KILO  
Protein Calories 10% Total Calories (M/40)

Men Age 30		Varying Size				
Description		Weight in Kg	Basal B	B + 50%	GM of Protein	GM Protein Per Kg.
<i>Short</i>						
5'	20% Underweight	46	1300	1950	48.7	1.0
	Normal	57	1420	2130	53.2	0.9
	20% Overweight	69	1540	2310	57.7	0.8
<i>Average</i>						
5' 8"	20% Underweight	55	1540	2310	57.7	1.0
	Normal	69	1700	2550	63.7	0.9
	20% Overweight	83	1840	2760	69.0	0.8
<i>Tall</i>						
6' 2"	20% Underweight	67	1760	2640	66.0	1.0
	Normal	84	1960	2940	73.5	0.9
	20% Overweight	100	2100	3150	78.7	0.8
<i>Men 5' 8" Normal Size</i>				<i>Varying Ages</i>		
Young	16 yrs.	62	1790	2685	67.1	1.1
Middle Age	40 yrs	72	1700	2550	63.7	0.9
Old	65 yrs	74	1620	2430	60.7	0.8

nished by diets containing basal plus 50% (diets for activity) and in which the protein calories constitute 10% of the total calories. It is obvious that when desugarizing diets of lower caloric value are used, the protein values per kilo also will be lower. In the

first part of each table nine combinations of height and weight are considered in a patient of 30 years of age. In the second section of the table, three widely different ages of an individual of average size are treated. It will be noted that the grams of protein

per kilo body weight fall below the value of one. By a similar computation these same relations may be shown to exist in the case of women.

If one should plan his diets on the basis of the theoretical weight for a given height rather than the actual weight, it will be noted that the protein value would reach 0.9 grams per kilo, which is sufficiently low to satisfy the demands of the advocates of low protein diets. It was therefore considered satisfactory to furnish the adult with a diet in which 10% of his total calories were derived from protein.

In the case of the child the problem is again complicated by the growth factor. Holt<sup>16</sup> states that healthy active children take 15% of their calories in the form of protein. He also states that 4 grams of protein per kilo body is taken in infancy and that this is reduced to 2 grams in adolescence. Bartlett<sup>9</sup> finds that the minimum protein for maintenance falls from 1.5 grams per kilo at 1

year of age to 0.6 grams at 14 years. G. L. Boyd<sup>10</sup> found that the minimum protein varied between 2.8 grams per kilo at 2 years to 1.25 grams at 10 years. This author states that for growth these values must be increased 10%. In diabetic children, Ladd<sup>8</sup> reported growth occurred in girls on diets which averaged 17.7% of calories from protein with a low value of 12.7%. Similarly boys grew on diets containing protein calories ranging from 12.1% to 20.8% with an average of 15.5%. Growth has occurred on levels of 1.5 to 2.0 grams per kilo. Talbot and associates,<sup>7</sup> Luther<sup>17</sup> and Peterman<sup>18</sup> in planning ketogenic diets have adopted 1 gram of protein per kilo body weight. As noted before the protein in these diets must be kept to the lowest limit compatible with health, so as to make the diet palatable.

Reference to Table II and III show that when 12½% of the total calories are fed as protein, and the more liberal caloric level of Holt and Fales is

TABLE II GRAMS PROTEIN PER KILO IN CHILDREN

*Protein Calories 12½% Total Calories (M/32)*

<i>Boys</i>					<i>Girls</i>			
Holt & Fales		Benedict & Talbot Basal & 100%			Holt & Fales		Benedict & Talbot Basal & 100%	
Wt in Kg	Total Calories	Protein per Kg Wt	Total Calories	Protein per Kg Wt	Total Calories	Protein per Kg Wt	Total Calories	Protein per Kg Wt
3	360	3.8	300	3.1	360	3.8	300	3.1
5	590	3.7	540	3.4	590	3.7	570	3.6
10	990	3.1	1090	3.4	990	3.0	1080	3.4
15	1300	2.7	1450	3.0	1260	2.6	1380	2.9
20	1600	2.5	1720	2.7	1520	2.4	1610	2.5
30	2400	2.5	2230	2.3	2370	2.5	2090	2.2
45	3600	2.5			3330	2.3		
60	3720	1.9			2640	1.4		
68	3265	1.5						

adopted, the grams of protein per kilo body weight corresponds to the optimal amount of protein indicated by the statistical studies of Holt and by the results in treating diabetic children as recorded by Ladd<sup>8</sup> and Boyd<sup>10</sup> In Table III the grams of protein per kilo body weight are shown, when the child is maintained at a somewhat lower level and the protein calories are estimated at 12½% of the total calories.

In Table IV the protein calories constitute 10% of the total calories, and the total calories correspond to basal plus 75% for boys and basal plus 50% for girls. The protein values derived in this table correspond more closely to those in use in the ketogenic clinics. Hence it is proposed that diabetic children be given 12½% of their calories in the form of protein, and that epileptic children under ketogenic management be given 10% or less of their calories as protein

TABLE III GRAMS PROTEIN PER KILO IN CHILDREN  
Protein Calories 12½% of Total Calories (M/32)

Weight in Kg	Boys			Girls		Protein Grams Per Kg
	Basal	Basal + 75%	Protein Grams Per Kg	Basal	Basal + 50%	
3	150	262 5	2 73	150	225	2 34
5	270	472 5	2 95	285	427 5	2 608
10	545	853 75	2 66	540	810	2 84
15	725	1268 75	2 64	690	1035	2 15
20	860	1505	2 35	805	1207 5	1 85
30	1115	1951 25	2 03	1045	1567 5	1 63

TABLE IV GRAMS PROTEIN PER KILO IN CHILDREN  
Protein Calories 10% of Total Calories (M/40)

Weight in Kg	Boys			Girls		Protein Grams Per Kg
	Basal	Basal + 75%	Protein Grams Per Kg	Basal	Basal + 50%	
3	150	262 5	2 18	150	225	1 87
5	270	472 5	2 36	285	427 5	2 13
10	545	853 75	2 13	540	810	2 02
15	725	1268 75	2 11	690	1035	1 72
20	860	1505	1 88	805	1207 5	1 5
30	1115	1951 25	1 62	1045	1567 5	1 3

THE GLUCOSE VALUE OF THE DIET  
AND THE KETOGENIC-ANTI-  
KETOGENIC RATIO

It is evident that if a diet must contain a certain number of calories and that if the protein calories are to com-

pose a definite portion of these total calories, that the glucose of such a diet will then be fixed when a given ratio of fatty acids to glucose is selected.

The chief criticism which may be made to the various published<sup>12 18 20</sup>

methods of diabetic diet adjustment, is the fixed ratio of fatty acids to glucose. More recently Wilder<sup>21</sup> has developed a method of diet calculation which gives a varying ratio. However, his calculations are all based on a fixed protein value of 50 which presents some objections. If a relatively mild diabetic presents himself for treatment, one might desire to use a high fat ratio in order to desugarize him rapidly without the use of insulin. If on the other hand, a case presenting a severe defect with an established ketonuria is encountered, it might be wiser to place the patient at once on a diet rich in carbohydrate (low fat ratio) and to supplement his tolerance with insulin. There are almost as many degrees of tolerance as there are patients. Hence it would be a great convenience to have available a simple method for calculating a diet with a ketogenic-antiketogenic ratio suited to the particular needs.

Evans<sup>22</sup> recognized this and proposed a method which allows one to pass from ratios of 1 to 4. However, he has to have a separate equation for the calculation of each constant. A simpler method would be more satisfactory. Ladd and Palmer<sup>3</sup> accomplished the same result by assuming that for all practical purposes the ketogenic amino acids in the protein molecule may be ignored. This same principle has been used in the calculation of ketogenic diets by Talbot, Metcalfe and Moriarty,<sup>7</sup> and Luther.<sup>17</sup> Perhaps the error involved in this assumption may not be great but it is nevertheless definite.

In one of his illustrative diets Woodyatt<sup>19</sup> observed that, if protein

be taken as 1 gram per kilo body weight and the fatty acid to glucose ratio be taken 15, the calories were 17 times the glucose value of the diet. It seemed wise therefore to generalize this into an expression from which a constant could be obtained that would be applicable to any desired ratio.

#### DERIVATION OF THE CONSTANT

The expression for this constant will be derived when the protein calories constitute 10% of the total calories. The basic assumptions are taken from Woodyatt's<sup>19</sup> discussion of the glucose and fatty acids in the diet.

The total calories (M) in the diet may be derived sufficiently accurately by multiplying the protein in grams (P) and the carbohydrate in grams (C) by 4, and the fat in grams (F) by 9.

$$(1) \quad M = 4C + 4P + 9F$$

The glucose (G) of the diet represents all the carbohydrate plus 58% of the protein plus 10% of the fat.

$$(2) \quad G = C + 58P + 1F$$

By transposing

$$(2a) \quad C = G - 58P - 1F$$

The fatty acids (F A) represent 46% of the protein plus 90% of the fat.

$$(3) \quad F A = 46P + 9F$$

By transposing and solving for F

$$(3a) \quad F = \frac{F A - 46P}{9}$$

The ratio (R) equals the fatty acids divided by the glucose

$$(4) \quad R = \frac{F A}{G}$$

$$(4a) \quad F A = R G$$



The protein calories are 4 times the protein in grams but they are also 10% of the total calories

$$\text{Protein calories} = 4P$$

$$\text{Protein calories} = \frac{\text{Total calories (M)}}{10}$$

$$4P = \frac{M}{10}$$

$$(5) P = \frac{M}{10}$$

The constant which we are seeking is a number which, when divided into the calories in the diet, will give the glucose of the diet.

$$(6) \frac{M}{K} = G \quad (6a) \frac{M}{G} = K$$

If now the value of C equation (2a) and P equation (5) be substituted in (1) we have

$$M = \frac{4(G - 58M - 1F)}{40} + \frac{4M}{40} + \frac{9F}{40}$$

By simplification

$$M = 4G + 0.42M + 8.6F$$

On substitution of the value of F equation (3a) and FA equation (4a)

$$M = 4G + 0.42M + 8.6(RG - 46P)$$

On simplification and substitution of value P in (5)

$$M = 4G + 9.55RG - 0.678M$$

$$M = \frac{G(4 + 9.55R)}{1.0678}$$

$$M = K = \frac{4 + 9.55R}{1.0678}$$

$$\frac{G}{K} = \frac{1.0678}{1.0678}$$

$$K = 8.943R + 3.746 \quad (10\%P)$$

As will be shown later the value of K will be sufficiently accurate if this expression is simplified into

$$K = 9R + 3.7 \quad (10\%P)$$

When the protein calories constitute 12½% of the total calories then it can be shown by a similar analysis that

$$P = \frac{M}{32}, \text{ and}$$

$$K = 8.803R + 3.687 \quad (12\frac{1}{2}\%P)$$

or more simply

$$K = 8.8R + 3.7 \quad (12\frac{1}{2}\%P)$$

#### CALCULATION OF A DIET BY USE OF THE CONSTANT

The usefulness of this constant may be best seen by a specific example: A patient requires 2,000 calories and it is considered advisable to use 12 ratio

$$K = 9R + 3.7 \quad (10\%P)$$

$$K = 9 \times 12 + 3.7 = 14.5 \quad (10\%P)$$

$$G = \text{Calories} = 2,000 = 137.9 = 138$$

$$\frac{K \text{ (constant)}}{14.5}$$

$$= \frac{137.9}{14.5} = 138$$

$$FA = G \times R$$

$$FA = 138 \times 12 = 1656$$

$$P = \frac{M}{32} = \frac{2,000}{32} = 62.5$$

$$F = \frac{FA - 46P}{9} = \frac{1656 - 2912.5}{9} = 158.4$$

$$C = G - .58P - 1F = 138 - 29 - 158.4 = 93.2$$

Calories calculated 1,998.4

Calories desired 2,000.

TABLE V. DIET FACTORS  
 $P = M/40$  and  $K = 9R + 37$   
 (10% P)

R	G	FA	C	P	F	Calories Obtained	Calories Desired	Error in Calories
1	126 0	126 0	90 8	40	119 5	1599 1	1600	0 9
3	52 1	156 3	13 6	40	153 2	1593 6	1600	6 4
1	157 5	157 5	113 5	50	149 4	1998 9	2000	1 1
3	65 2	172 4	17 0	50	191 6	1992 1	2000	7 9
1	252 0	252 0	181 7	80	239 1	3198 2	3200	1 8
3	104 2	312 7	27 2	80	306 5	3187 6	3200	12 4

TABLE VI DIET FACTORS  
 $P = M/32$  and  $K = 88R + 37$   
 (12½% P)

R	G	FA	C	P	F	Calories Obtained	Calories Desired	Error in Calories
1	128 0	128 0	87 3	50 0	116 7	1599 3	1600	0 7
3	53 1	159 4	8 9	50 0	151 5	1598 4	1600	1 6
1	200 0	200 0	136 5	78 1	182 3	2498 9	2500	1 1
3	83 0	249 1	14 0	78 1	236 9	2500 8	2500	0 2
1	256 0	256 0	174 7	100 0	233 3	3198 7	3200	1 3
3	106 3	318 9	18 0	100 0	303 2	3201 2	3200	1 2

Reference to Table V shows that over a range of ratios from 1 to 3, and over a range of calories from 1,600 to 3,200, when  $K(10\%P) = 9R + 37$ , the maximum adjustment is 12 4 calories. In Table VI over the same range when  $K(12\frac{1}{2}\%P) = 88R + 37$ , the maximum adjustment is 1 3 calories.

It is therefore evident that by remembering the equation for the derivation of these two constants, a diet with any given number of calories and ratio may be simply and directly derived.

#### CALCULATION OF THE RATIO OF THE METABOLIZING MIXTURE DURING DESUGARIZATION

Another application of this method of calculation will be cited.

A patient enters the hospital showing a moderate ketosis. Certain ques-

tions arise. Can he be desugarized by diet adjustment alone? To what level must the glucose be reduced? Can such a desugarization be attempted with safety?

The basal requirements of the patient are 1,400 calories. This is the lowest level at which the weight can be maintained, and experience has shown that this quantity of energy will be completely used. We may then with confidence state that this is a close approximation of the caloric value of the metabolizing mixture. So the patient is placed on a diet of carbohydrate 60 gms, protein 35 gms, fat 113 gms, which yields a glucose of 91 6 gms, a fatty acid value of 118 gms, a ratio of 1 28 and calories 1,397. On such a diet he excretes 34 gms, 30 gms, and 32 gms, on successive days. The urine contains both acetone and diacetic

acid. His plasma carbon dioxide is 54. His average glucose excretion then is 32 gms per day, and his present tolerance is (91.6 — 32) 59.6 gms

We may now calculate the ratio of fatty acids to glucose in his metabolizing mixture

$$\frac{M \text{ (Total Calories)}}{K \text{ (constant)}} = G \text{ (Glucose)}$$

$$\frac{1400}{K} = 59.6$$

$$\begin{aligned} 1400 \\ \text{---} &= K = 23.5 \\ 59.6 \\ 9R + 37 &= K \\ 9R + 37 &= 23.5 \\ 9R &= 19.8 \\ R &= 2.2 \end{aligned}$$

This should be a perfectly safe ratio. Wilder<sup>1</sup> and Shaffer<sup>23</sup> have shown that theoretically one molecule of glucose can catalyze the oxidation of two molecules of fatty acids or 1 gm. of glucose 3 gms. of fatty acids. Beyond this limit the diabetic organism cannot compensate for extra fatty acids which are produced and remain unburned. In other words a fatal acidosis will supervene.

It is an established plan in desugarizing by diet adjustment to reduce the glucose definitely below the patient's known or estimated tolerance. Hence the glucose in this case should be reduced to 50 gms. What would be the effect of such a reduction on the ratio? By a similar computation it can be shown that the ratio would now be raised to 2.7, which is just inside the maximal limit.

One may conclude that if the pa-

tient is not an arterio-sclerotic diabetic that he can be desugarized by reducing his glucose intake to 50 gms; but that on such a diet the patient is called on to burn a metabolizing mixture, which contains a maximal quantity of fatty acids and for this reason the factor of safety in it is indeed small.

### CONCLUSIONS

The principles underlying the calculation of flexible diets may now be summarized.

1. In adults the total calories fed during periods of desugarization vary between basal and basal plus 30%, and during activity between basal plus 50% and basal plus 75%. In children desugarizing diets should contain basal plus 30% calories. Diets adequate for growth and activity contain, in the case of boys, basal plus 75% calories, and in the case of girls, basal plus 50%.

2. In the adult the calories derived from protein constitute 10% of the total calories; in diabetic children, they constitute 12½% of the total calories. In children, under treatment with a ketogenic diet, the protein calories constitute 10% or less of the total calories.

3. When the protein calories are 10% of the total calories, an expression for a constant K was derived.

$$K = 9R + 37 \\ (10\%P)$$

Now any desired value may be assigned to R (ratio) and the diet calculated by substitution in the expression

$$\frac{\text{Total Calories}}{K \text{ (Constant)}} = \text{Glucose} \\ (10\%P)$$

Once the ratio has been selected and the glucose calculated, the carbohydrate and fat can be easily derived

4 When the protein calories are  $12\frac{1}{2}\%$  of the total calories, the expression for the constant becomes.

$$K (12\frac{1}{2}P) = 88R + 37$$

5. Such a constant is also helpful in

computing the ratio of fatty acids to glucose, metabolizing at any given period during the process of desugarization.

6 Diets calculated according to these formulas give the desired calories without secondary re-adjustments.

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# Studies on the Diagnosis of Pancreatic Disturbances\*

## I. Methods of functional diagnosis

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THE present communication relates to the diagnosis of diseases of the pancreas. In it are reviewed the procedures and methods proposed as diagnostic aids and their status discussed.

Pancreatic disease has usually been considered as of infrequent occurrence. Cammidge (1) was one of the first to question its infrequency. In 1911 he wrote as follows: "Since 1900 it has been gradually recognized that chronic pancreatitis is a much more common disease than had been formerly supposed, but even yet there is a tendency to regard it as of theoretical rather than practical interest. This is far from being the case. My experience during the past ten years has convinced me that it is a very real disease and I feel sure that if it were more frequently diagnosed in the early stages, when treatment is of most avail, much needless suffering and even loss of life might be avoided. Its clinical importance lies not so much in its early symptoms as in the effects it may produce if allowed to progress unchecked."

Surgeons frequently diagnose the presence of pancreatic involvement by palpation during laparotomy. How much the surgeon can accurately determine concerning the state of the pancreatic gland through its palpation is an open question (2). Nevertheless, those of us whose work brings us into intimate contact with him soon learn that his palpating fingers possess a wonderful acumen in detecting pathologic anatomy within the opened abdomen. Whether or not Cammidge and other observers have been correct in diagnosing the presence of pancreatic involvement by the various methods employed by them also is admittedly an open question. Thus, the diagnosis of pancreatic disease is frequently based on evidence of uncertain status. However, it is at least suggestive enough to warrant further investigation.

A number of procedures have been proposed for the purpose of eliciting evidence of pancreatic involvement. Critical review of them demonstrates that they are designed to show functional disturbances in the pancreas either directly or indirectly through the secondary effects on metabolism. They may be classified as follows:

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## I. Direct tests for pancreatic function.

### A. The estimation of the concentration of pancreatic enzymes in vitro (quantitative).

#### 1 Estimation in excreta

- (a) Trypsin in feces<sup>3 4 5</sup>
- (b) Diastase in feces<sup>6 7 8</sup>
- (c) Lipase in urine<sup>9</sup>
- (d) Diastase in urine<sup>7</sup>

#### 2. Estimation in gastric contents

- (a) Trypsin, diastase and lipase after an oil meal<sup>10 11</sup>

#### 3. Estimation of enzymes in duodenal contents<sup>12 13 14 15</sup>

#### 4 Estimation in blood

- (a) Diastase<sup>7 16</sup>
- (b) Lipase<sup>17</sup>

### B The estimation of the concentration of pancreatic enzymes in vivo

#### 1. Keratin coated capsules containing methylene blue<sup>18</sup>

#### 2. Glutoid capsules of Sahl containing iodoform<sup>19</sup>

#### 3 Nucleus test of Schmidt,<sup>20</sup> and the modifications of Einhorn,<sup>21</sup> and Kashiwado<sup>22</sup>

## II. Test for demonstrating the secondary effects of pancreatic function on metabolism

### A. Effect on carbohydrate metabolism

#### 1. Glycosuria

- (a) Dynamic
- (b) Potential

#### 2 Cammidge pancreatic reaction<sup>23</sup>

### B. Unclassified effect on metabolism

#### 1. Loewi mydriasis test<sup>24</sup>

### C. Effect on alimentation

#### 1 Steatorrhea and percentage of undigested fats<sup>2 25 26</sup>

#### 2 Azotorrhea and creatorrhea<sup>27 28</sup>

#### 3 Urinary ethereal sulphates

Only the basic principles of the methods above outlined are required for purposes of the present discussion. An intimate description of most of them will be found in the publications of Pratt,<sup>2</sup> Sladden,<sup>27</sup> Spriggs and Leigh,<sup>18</sup> Decker<sup>28</sup> and Wallis<sup>29</sup>

## DISCUSSION OF THE CLINICAL SIGNIFICANCE OF TESTS FOR PANCREATIC FUNCTION, DIRECT FUNCTIONAL TESTS IN VITRO

Procedures proposed for the purpose of determining the action of pancreatic enzymes in vitro may be divided into two general classes as follows (a) those which incorporate the proper physicochemical conditions governing enzymic action, and (b) those disregarding such conditions. Sorenson<sup>30</sup> has established the physicochemical conditions governing the activity of enzymes.

One of the few means for quantitating an enzyme is by determining its concentration. The concentration may be established indirectly by measuring the activity of the enzyme under a given set of experimental conditions. If the degree of activity is to be the index of an enzyme's concentration in different media, the method for estimating such activity must operate under the physicochemical conditions

which will produce the following phenomena. (1) uniformity of enzymic action, (2) proportionality of enzymic activity; (3) stability of the enzyme, and (4) homogenous physical state of the medium on which the enzyme is to act. A fifth important condition relates to the quantitative accuracy and delicacy of procedures for estimating the amount of enzyme action. The action of an enzyme is considered uniform when under a given set of experimental conditions similar results with a certain specimen containing the enzyme are obtained in repeated analyses. Uniformity of enzymic action is obtained by the proper concentration of hydrogen ions maintained by suitable buffer conditions. These same conditions govern proportionality of enzymic action, and unless they are proper the proportionality of enzymic action will be very slight. Obviously, the stability of an enzyme in relation to the length of time its action is to be measured must be considered in any method for demonstrating uniformity or proportionality of enzymic activity. This means that the action of the enzyme studied must be approximately as great at the conclusion of an experiment as it was at the beginning of the same, i.e., the concentration of the substrate must remain practically unaltered. The physical state of the medium on which the enzyme acts must be constant if uniformity of action is to be obtained. One essential reason for this is the fact that the size of the surface area of material exposed to enzyme action is an essential factor governing the amount of the latter. The proper physical conditions may be obtained by means of solutions or by

emulsions so finely divided as partially to resemble colloidal suspension.

Hawk<sup>8</sup> used buffer salts in his method for determining the amylolytic concentration of stools. Unfortunately, all other methods described for estimating pancreatic enzymes in urine, stools or in gastric contents have disregarded buffer and hydrogen ion conditions. Disregard of these physicochemical conditions destroys proportionality of enzymic action, indeed it may permit a very low enzymic concentration to show more relative activity than one of much greater degree. Obviously, such results would lead to entirely erroneous clinical interpretation if the degree of activity is used as an index of enzymic concentration. Therefore, these methods are of insignificant clinical value. The method proposed by Hawk<sup>8</sup> for the estimation of diastatic concentration of feces would probably give good results were the procedure for determining the degree of action on the starch sufficiently accurate and delicate. In order to gain simplicity Hawk uses the well known Wohlgemuth<sup>7</sup> series of tubes containing starch. None of the chemical procedures necessary for determining accurately the concentration of the starch solution are used. Obviously therefore, the actual amount of starch acted on by the enzyme would be uncertain. Furthermore, relatively concentrated fecal extracts must be used, which destroys the delicacy of the method. Also, bacteria compose an appreciable proportion of feces. These bacteria give rise to enzymes which have the same action as those of pancreatic origin. These various factors detract greatly from the clini-



cal value of the results obtained by Hawk's method

Except for the casein solution used by Gross<sup>4</sup> the substrata employed in determining either proteolytic (trypsin) or lipolytic (lipase) activity of urine, stools, or gastric contents have not been homogenous. Lack of homogeneity of such substrata permits tremendous variations in the degrees of activity of the enzymes. All the methods use procedures for determining the quantity of the product of enzyme action which are open to gross errors. The source of these errors are too apparent to necessitate their description. From this discussion it is obvious that the methods proposed for demonstration of pancreatic insufficiency by determining enzymic action in urine, stools and gastric contents can only give results of most uncertain reliability. Application of these methods to clinical medicine has been found to be of insignificant value by McClure and Pratt,<sup>31</sup> Pratt,<sup>3</sup> Spriggs and Leigh,<sup>18</sup> Wallis,<sup>29</sup> Sladden,<sup>27</sup> and others.

The determination of various enzymic concentrations of blood has been proposed as a means for estimating the activity of external pancreatic secretion. Wohlgemuth<sup>7</sup> applied his method for estimation of diastatic activity of urine to the blood. Unfortunately, here as in the urine, the method does not call for the use of buffer salts. Consequently enzymic action is not uniform and the results obtained give no conception of the true concentration of the diastase present in the blood serum. Obviously, clinical interpretation of such results can not be safely made. Myer<sup>16</sup> has de-

vised a method for determining diastatic concentration of the blood. Chemically the method is correct except that the media used are not buffered. In view of the studies carried out by Sorenson<sup>10</sup> and of unpublished observations by Wetmore and McClure, it is doubtful whether uniformity of enzymic action of blood will be obtained in the absence of buffered solutions. This observation renders the results obtained by Myer's<sup>16</sup> method problematical.

Rona and Pavlovic<sup>17</sup> report that the activity of lipase of pancreatic origin is much less inhibited by atoxyl than lipase from other sources. On the basis of this observation they claim to have demonstrated pancreatic lipase in the blood, and propose its determination as an index to the activity of external pancreatic function. Kivilecki<sup>32</sup> has applied the method reported by Rona and Pavlovic clinically and concludes that it is of significance in the diagnosis of external dysfunction of the pancreas. However, the method proposed by these investigators does not incorporate those physicochemical conditions controlling enzyme action. Therefore, in spite of Kivilecki's conclusions, further investigations will be necessary before the clinical status of the procedure is established.

Einhorn<sup>33</sup> and Gross<sup>34</sup> have independently devised tubes by which contents from the duodenum can be obtained. Theoretically these contents could be examined for their enzymic concentrations and in this way one of the pancreatic external functional activities determined directly. Einhorn,<sup>14</sup> and Hollander and Mann<sup>12</sup> devised methods for the estimation of such

enzymic activities. However, their methods did not call for the use of buffered conditions and are open to the serious objections previously discussed. Bassler<sup>13</sup> devised a relatively simple method for the estimation of the concentration of the diastase present in duodenal contents. Unfortunately, the procedure for quantitating the end result is the inaccurate one proposed by Wohlgemuth,<sup>7</sup> while the solutions are improperly buffered. Furthermore, the highly important proteolytic and lipolytic functions of the pancreas are not determined. Obviously, it would be unsafe to rely on results obtained by this method, except perhaps in the presence of far advanced disease of the pancreas.

Recently Okada, Sakurai, Imazu and Kuramochi<sup>15</sup> have proposed new methods for estimating concentration of the enzymes of duodenal contents. They employed ether, alcohol, water and hydrochloric acid as stimulants to the secretion of pancreatic juice. These stimulants were used possibly because Okada and associates were apparently uninformed concerning the extensive investigations of McClure and coworkers<sup>35 36 37 40 42</sup> on the mechanisms of pancreatic stimulation. The latter have established beyond all reasonable doubt that in man adequate amounts of the products of the digestion of foodstuffs are the *only* substances which will *uniformly* stimulate the flow of pancreatic juice. Therefore, the specimens of duodenal contents analysed by Okada and coworkers represented the enzymic concentrations common to the fasting state plus whatever additions occurred as the re-

sult of widely variable degrees of pancreatic stimulation.

The Japanese investigators further conclude that 94 to 99 per cent of contents of the duodenum can be regularly collected through the duodenal tube by suction. However, McClure and Reynolds<sup>37</sup> made numerous observations which demonstrated conclusively that material can be aspirated from the duodenum only when the suction is applied coincidentally with the occurrence of duodenal peristalsis. Fluoroscopic observations showed that materials entering the duodenum quickly passed the duodenal tube, so that only indefinite amounts could be recollected through the tube either by siphonage or aspiration. These observations showed that aspiration has no advantage over siphonage. Furthermore, the method employed by the Japanese investigators for estimating the amount of material recollected through the tube was a colorimetric one, based on the determination of the concentration of phenolphthalein. The admixture of bile present in duodenal contents destroys the accuracy of such a determination. The physical conditions governing the proper use of the colorimeter are such that all solutions to be compared must be absolutely clear and of the same shade of color. Any juggling of the solutions in order to make the shades similar, as was done by the Japanese workers, can only lead to the grossest errors. Therefore, the method used by them does not ascertain what proportion of the contents of the duodenum can be collected through the duodenal tube. These observations show the futility of their attempts to estimate the

amounts of enzymes secreted by the pancreas from calculations involving the total amounts of duodenal contents

McClure and Wetmore, as a basis for their work on duodenal enzymes, made extensive studies on the physicochemical conditions governing uniformity and proportionality of the action of such enzymes. These studies included observations on phosphate mixtures representing wide ranges of molecular and hydrogen ion concentrations. During such studies it was demonstrated conclusively that the ultimate molecular concentrations of phosphate mixtures proposed by Okada and associates do not produce either uniformity or proportionality of enzymic action.

The Japanese investigators did not locate the position of the duodenal tube by radiographic means before collecting duodenal contents for analysis. Material indistinguishable in its physical appearance from duodenal contents has often been obtained from the pyloric end of the stomach by the present author. Such observation demonstrates the impossibility of ascertaining the source of material returned through the duodenal tube unless the exact position has been determined fluoroscopically.

The data presented above demonstrate that the results obtained by the methods and procedures proposed by the Japanese investigators are subject to uncontrolled variables. The variables which most adversely affect the reliability of the results are as follows: (1) variable degrees of stimulation of the flow of pancreatic juice, (2) variability of calculated enzymic

concentrations due to differences in the proportionate amounts of duodenal contents; (3) variability of enzymic action due to absence of physicochemical conditions producing uniformity and proportionality of such action; and (4) variable sources of the duodenal contents, from either the stomach or the duodenum. Obviously, all these variables render the results obtained highly difficult of interpretation. The effects of the variables discussed were observed by Okada and associates, but their cause was apparently not recognized. They attempted to overcome them by collecting duodenal contents over a period of three hours. They were apparently unaware that McClure and coworkers<sup>30, 37</sup> demonstrated that, when the proper pancreatic stimulants are used, the various hourly fractions of duodenal contents collected throughout periods of 5 and 6 hours give comparable results.

From the above discussion it is obvious that all the methods and procedures discussed for estimating pancreatic functional activity through determination of enzymic action give results which are of highly problematical value.

#### DIRECT FUNCTIONAL TESTS IN VIVO

Capsules which contain chemicals, that appear in the urine after absorption from the intestine, have been proposed as tests for pancreatic function. Such capsules are coated with some substance resistant to gastric digestion but which may be dissolved by action of pancreatic juice. The two best known capsules are the keratin coated capsule containing methylene blue and the formalin hardened gelatin capsule.

containing iodoform. However, the recent widespread use of coated pills and capsules for x-ray purposes serves to demonstrate how frequently such capsules or pills are not broken up in the small intestines. This observation renders highly problematical the significance of results obtained by the pancreatic test capsules. In actual practice this has been found to be the case by Wallis,<sup>20</sup> by Sladden,<sup>27</sup> by Spriggs and Leigh,<sup>18</sup> and Pratt.<sup>2</sup>

The sajodin test of Winternitz depends upon the splitting up of an iodized oil in the intestines and the subsequent elimination of iodine in the urine. The theoretical value of this test was based on the assumption that the iodine would not be liberated in the absence of pancreatic juice. However, McClure, Vincent and Pratt,<sup>20</sup> showed that fats are split up in the intestines in the complete absence of pancreatic juice. This renders the utility of the sajodin test very doubtful. The cube beef test of Schmidt consists of feeding beef in a mushin sac, recovering it from the stools and examining the degree of nuclear preservation. This test is of clinical significance in the complete absence of pancreatic juice. Einhorn,<sup>21</sup> and Kashwado<sup>22</sup> have made minor modifications of the test. The nuclear test is, therefore, the only one of those designed to show pancreatic enzymic action *in vivo* which is of practical utility.

#### TESTS DEMONSTRATING METABOLIC DISTURBANCES

Glycosuria, the Cammidge<sup>23</sup> pancreatic reaction, Loewi's<sup>24</sup> adrenalin mydriasis test and the observation of

increased ethereal sulphates in the urine are phenomena common to disturbances other than involvement of the external secretory function of the pancreas. This factor is sufficient to render difficult their interpretation in relation to affections of the pancreatic parenchyma. Nevertheless, glycosuria and the Cammidge reaction are occasionally of some value in deciding the question of destructive lesions of the pancreas.

In the absence of jaundice, grossly fatty stools are indicative of extensive disease of the pancreas or of marked pancreatic dysfunction, such as occurs in congenital steatorrhea. In creatorrhea, large amounts of microscopically well preserved muscle fibers, and azotorrhoea, high nitrogen content of the stools, are also present, then the condition is almost certainly one of very far advanced pancreatic insufficiency. At such a time the stools may show a large percentage of undigested fat. However, in the presence of marked disease of the pancreas,<sup>27</sup> or in its entire absence,<sup>20</sup> analysis may demonstrate little disturbance in fat digestion. Therefore, the absence of excess fat in the stools does not rule out the presence of pancreatic dysfunction. The proper examination of stools requires a complete metabolism experiment. This includes analysis of food ingested, collection of feces over a period of several days and their ultimate chemical analysis. Such an extended investigation is rarely of sufficient clinical value to be justifiable.

The following conclusions may be safely drawn from the foregoing discussion of the various pancreatic functional tests proposed.

- 1 All methods discussed for the estimation in vitro of enzymic concentration of urine, stools, blood and duodenal contents are subject to serious chemical and physico-chemical omissions of such nature that results obtained by them are difficult if not impossible of exact clinical interpretation
- 2 The demonstration of the absence of pancreatic trypsin in vivo by the nucleus test of Schmidt is of practical utility in far advanced pancreatic disease. The capsule and iodized oil tests are of insignificant value
- 3 Examination of the stools by the methods outlined are of practical utility in the diagnosis of conditions representing far advanced pancreatic dysfunction. Glycosuria and the Cammidge reaction are occasionally of practical value as indirect symptoms of external pancreatic involvement. The other methods for showing disturbances in metabolism secondary to pancreatic insufficiency are of doubtful utility

The foregoing discussion shows the need for means of certainly ascertaining both minor and advanced degrees of disturbances in the state of pancreatic function. One of the most promising means for obtaining information concerning an organ's functional condition is the study of that organ's secretions. The digestive secretion of the pancreas is found in the duodenum, from which it may be obtained by means of the usual tube. McClure and coworkers have devised procedures for obtaining suitable specimens

of duodenal contents and methods for their analysis. In order to obtain duodenal contents containing pancreatic juice representative of that secreted during the intestinal digestion of food it was necessary first to establish the usual physiologic mechanisms concerned in the stimulation of the external functional activity of the pancreas. The investigations<sup>38</sup> carried out on these mechanisms demonstrated that the products of food digestion were the usual stimulants to the secretion of pancreatic juice. In the course of animal studies it was demonstrated that, under suitable experimental conditions, introduction of the products of food digestion into either the femoral or mesenteric veins would stimulate the secretion of pancreatic juice. These observations on animals fully confirmed those made on man. Of the various food products, cream<sup>37</sup> or oleic acid<sup>38</sup> has been found most suitable for use in the procedure developed for collecting specimens of duodenal contents for analysis. The use of oleic acid permits examinations of the bile moiety<sup>42</sup> as well as of the pancreatic fraction. The state of the alkali secretory function of the pancreas is estimated as the buffer values of duodenal contents. The activity of the enzyme secretory mechanism is estimated by determining the concentration of three pancreatic enzymes present in duodenal contents.

The buffer values<sup>39</sup> of duodenal contents are determined by use of the potentiometer. Fifty cc of the contents are titrated with tenth normal hydrochloric acid or sodium hydroxide solution, according to whether the original material was alkaline or acid. The re-

sulting pH values are determined up to and beyond the neutral point. Curves of these values are plotted against the amount of acid or alkali, and the amounts needed to bring the pH value to 7 are read from the curves. Further buffer values are computed from the equation developed by Van Slyke

$$B = \frac{\Delta B \text{ or } \Delta A}{\Delta \text{pH}}$$

$\Delta B$  or  $\Delta A$ , is the amount of tenth normal alkali or acid required to neutralize 1 cc of duodenal contents, or

$$\Delta B, \text{ or } \Delta A = \frac{V \quad N}{V} \text{ in which } V$$

is the volume of the alkali or acid used,  $N$  is the normality of the solution, and  $V$  the total volume of the

original duodenal contents in the titration vessel. The total change in the pH value from the original to the neutral state is  $\Delta \text{pH}$ . Methods<sup>10</sup> have also been devised for determining the enzymic concentration of the pancreatic fraction of duodenal contents. These methods incorporate all the chemical and physico-chemical principles which insure delicacy, uniformity and proportionality of enzymic activity. Also, the procedures for the estimation of the amounts of enzyme action give accurate results. Uniformity and proportionality of enzymic activity have been obtained by regulating the latter with phosphate mixtures. The amount of enzyme action for the proteolytic and amylolytic enzymes is estimated by application of the methods of Folin for nonprotein nitrogen

and sugar in the blood. The activity of the fat splitting enzyme is estimated by determining the degree of acidity developed in a true emulsion of olive oil or of cottonseed oil, by titrating while hot with alcoholic potash solution, using phenolphthalein as an indicator. The delicacy of the methods is such that the enzymic concentration of 0.02 to 0.04 cc of duodenal contents is determined.

Initial observations<sup>36, 37</sup> on normal subjects established the activities of the pancreatic enzymes present in duodenal contents. Later these observations were fully confirmed by studies made by Jones<sup>41</sup>. Subsequent to the work of Jones, the author has added confirmation to all these observations by a study of a much larger series of control observations<sup>42</sup>. The results of studies<sup>43</sup> made on enzymic activities of duodenal contents in patients with unquestionable disease of the pancreas, many of whom came to autopsy or laparotomy, established the clinical value of such determinations. The results of these studies were confirmed later by observations<sup>42</sup> on a much larger number of patients. Sufficient numbers of observations have been made definitely to eliminate the various sources of error which were theoretically objectionable. When the proper portion of duodenal contents has been collected and the analytical methods have been correctly performed the results obtained give uniformly reliable information concerning the external secretory activities of the pancreas.

When the enzymic concentrations of duodenal contents is used as the index of activity of the external func-

tions of the pancreas, such concentrations fall into three groups as follows

- 1 Normal concentrations are found in all conditions in which the functional activity of the pancreas is unimpaired
- 2 Abnormally low concentrations are found in lesions including the ampulla of Vater, lesions involving the head of the pancreas and in acute or chronic pancreatitis
- 3 An intermediate value between normal and abnormally low concentrations is characterized by normal concentrations of one or two enzymes, while that of the other one or two is much diminished below the minimum normal, that is, dissociation of the secretion of the various types of enzymes occurs. This is found in convalescence from acute pancreatitis, in functional impairment accompanying partial occlusion of the ampulla of Vater and also during stages of destructive lesions involving the pancreas. Jones<sup>41</sup> demonstrated such dissociation in diabetes mellitus.

McClure and coworkers therefore have established the following

- 1 The usual physiologic mechanisms concerned in the stimulation of the digestive activities of the pancreas
- 2 Procedures for obtaining duodenal contents representative of

pancreatic juice secreted during intestinal digestion.

- 3 Methods of determining with a high degree of accuracy the states of activity of the enzyme and alkali secretory functions of the pancreas
- 4 Physiological variations of the enzymic and alkali functional activities of the pancreas
- 5 Variations in the enzymic concentrations in the duodenal contents in the presence of abnormal pancreatic function
- 6 A clinical status for the results obtained by the use of the procedures and methods for determining the enzymic concentrations of duodenal contents

By the use of these methods and procedures pancreatic dysfunction can be ascertained in its incipency, as well as when far advanced

#### SUMMARY AND CONCLUSIONS

Most tests designed to estimate the activity of the pancreas are based on erroneous physical and physico-chemical conditions. These conditions are so erroneous as to render the tests almost valueless. The nuclear test and certain metabolic examinations are of value in demonstrating far advanced disease of the pancreas. The presence of glycosuria and a positive Cammidge pancreatic reaction in the urine are of varying degrees of diagnostic aid. McClure and coworkers have devised means for accurately demonstrating pancreatic dysfunction of both mild and advanced degrees.

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# The Treatment of Acute Asphyxia\*

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THE subject I have to speak about is one of which I have had an exceptional chance during the past five or six years to become familiar with, and one which in its acute aspects the medical profession usually meets after something or other has been done by laymen

Acute asphyxiations in the registration area of the United States cause about 14,000 deaths a year. The principal conditions in which acute asphyxia occurs are drowning, which makes almost 7,000 of these deaths, carbon monoxide poisoning, which makes about 6,000 more, and electric shock, which completes the total

I want to speak first of all about carbon monoxide poisoning, in which I have been particularly interested. In 1920, at the request of the American Gas Association, I formed a commission to study methods of resuscitation from carbon monoxide poisoning. I was greatly surprised by the amount of such poisoning in fatal form which occurs in our large cities. In New York City, for example, exclusive of Brooklyn, the emergency service of the New York Gas Company is called to an average of 1,600 cases of carbon monoxide poisoning a year, with about 800 fatalities. Somewhere in the neighborhood of 45 per cent of these are suicidal. In prac-

tically every instance they are seen by laymen before a physician is called, but as soon as the physician reaches the case, he is in entire charge, and all other agencies are subservient to him.

It is an interesting commentary on the knowledge of the medical profession of the actual condition of persons who are seriously asphyxiated either from carbon monoxide poisoning, drowning, or electric shock that I have in my possession the records of nine cases where physicians have pronounced the individual dead. In two cases he turned the body over to the coroner, and in almost every instance fellow workmen continuing efforts of artificial respiration have succeeded in bringing back a complete recovery.

It is quite obvious that most physicians are not familiar with the degree to which circulatory activity can continue to persist in an individual in a very restricted area for a fair period of time and under circumstances which, with the finger and a stethoscope, are almost entirely beyond methods of detection.

If one takes the course of a case of carbon monoxide poisoning, certain interesting things happen which are related very directly to the method of treatment to be applied. When one breathes a low concentration of carbon monoxide, let us say a quarter of a per cent of carbon monoxide gas in the air of a room—and for your information, in order to have some basis

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for comparison the ordinary Ford car running in a closed garage, producing from 7 to 9 per cent of carbon monoxide in the gas in the exhaust, will develop an atmosphere which should be fatal within 5 to 6 minutes.

There is invariably a period of hyperpnea of varying length, depending on the rate at which poisoning occurs. During this period of hyperpnea with the individual wholly quiescent, carbon dioxide is progressively lost, so that the individual is projected slowly, fairly slowly, usually, into a condition of alkalosis. The  $\text{CO}_2$  carrying power of the blood may be reduced after such a period, owing to the fact that bicarbonate has diffused from the vessels into the tissues. He is, however, in spite of this loss of alkali from the blood, in a condition of alkalemia. He is slowly moving over into a position in which respiratory stoppage is more or less inevitable.

What the cause of hyperpnea in carbon monoxide poisoning is certainly cannot be said with final assurance. It does not seem justifiable to me to attribute it wholly to the development of anoxemia. However, we find as the breathing begins to fail an individual, he is not only walled off from oxygen by the combination of carbon monoxide with his hemoglobin, but is in a position to help himself practically not at all as regards the intake of oxygen from the air. On the basis of this situation, Dr. Henderson and his co-worker Haggard recommended as their share of the work of our commission that these individuals be given an inhalation of carbon dioxide in order to supply the carbon dioxide which had been breathed out, and to stimulate breathing in a natural man-

ner. With this carbon dioxide, following the very old method treatment, 95 per cent of oxygen was combined. The individual's breathing was thus stimulated by carbon dioxide and he took such a high concentration of oxygen as to increase the oxygen in his alveolar air and to hasten the disassociation of the carbon monoxide hemoglobin in the best manner possible. That treatment was put in actual operation in the United States in 1923. It is now possible to say that in practically all the large and many of the small cities in the country this mixture of 95 per cent oxygen and 5 per cent carbon dioxide can be placed at the disposal of physicians, usually by the local gas or electric companies who keep apparatus suitably designed and approved for us by a commission now in existence on the part of the American Gas Association, so that the apparatus may be safely used by the lay crews who are handling them.

In a case of carbon monoxide poisoning, which is reached soon by a physician in any one of the large cities, this simple physiological method of treatment can be reached at once. In New York City, for example, there are six, twenty-four-hour emergency stations so equipped, all within the call of anyone who may need such help. Here in Boston and vicinity the same is true, and so it goes throughout the country.

This treatment of gas asphyxiation, physiologically grounded, is apparently ideal, yet it has not succeeded quite as well in some instances as it should. The reason for this was not apparent to us until the past year. If one takes a group of normal subjects and has them breathe a mixture of 5 per cent

carbon dioxide and air, he finds to his surprise that every individual increases his minute volume to a different degree and at a different rate. We have known clinically that this occurred in certain degree in hypertension with arteriosclerosis, but the degree of variation which exists between different individuals and the rate and extent to which they increase their breathing when confronted with 5 per cent carbon dioxide certainly was quite unfamiliar to me. More interesting than this, and contrary to the literature as it now exists, the same individual breathing this mixture on different days responds quite differently. Let us speak of experiments within the past couple of weeks. For example, I myself breathing 5 per cent  $\text{CO}_2$  increased my minute volume to 41 liters on one day. Five days before that, under conditions of health, as far as I could see, identical, my breathing increased to but 23 liters per minute. Therefore, when one takes 5 per cent carbon dioxide in apparent good health, for reasons which as yet are unexplored, the extent of the response in different individuals is quite different and the extent of the response in the same individual, contrary to past opinion, varies from day to day. While it is by no means proved, and probably extremely difficult to prove, it seems to me that this result indicates a variation in the threshold of the respiratory center for stimulation. That is to say, an equivalent hydrogenized concentration acting as the stimulating agents of the respiratory center operates with different degrees of vigor at different times in the same apparently healthy individual.

It is an interesting fact that if ani-

mals are given carbon monoxide to breathe and their response as asphyxia from the carbon monoxide develops, in terms of increased breathing to 5 per cent carbon dioxide inhalation, is measured, that as the asphyxiation progresses the response of the individual rapidly tends to decrease, so that in the most serious conditions of poisoning, when we really require stimulation of breathing, we have an individual whose threshold for stimulation has fallen and we have found that it is essential to begin the inhalation on such persons with a higher concentration. Seven to ten per cent is now being tried in the field, with very interesting results, and results in accord with some of the recent work on the inhalation of high concentrations of carbon dioxide in patients in catatonic states. I now have records of several cases with a return of consciousness, actual speech, on 7 per cent carbon dioxide. With a shift to the 5 per cent of carbon dioxide oxygen application, you will have a lapse into unconsciousness again after a few minutes, with a further recovery when put upon the higher concentration. It is thus evident that in the treatment of carbon monoxide poisoning the concentration of carbon dioxide used, as these cases reach the hospital and inhalation treatment is frequently available, should be increased and freely increased when the men are first seen by the physicians in charge.

Other details in regard to treatment with drugs are of little importance. I may mention only one very necessary precaution into which I cannot go into detail. It is that atropin is a decidedly dangerous drug for such individuals.

# The Use of Sodium Salt of Dehydrocholeic Acid (Decholin) as a Choleric\*

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M.D., Division of Medicine, *The Mayo Clinic, Rochester, Minnesota*

NEUBAUER has been foremost in the investigation of a sodium salt of dehydrocholeic acid that would stimulate the liver to increased formation of bile. Most investigators have shown this drug to be practically without toxic effects and that it markedly increases the flow of bile. Our investigation was undertaken to see if we could obtain results comparable to those reported by Neubauer, Ruzsnyák and others.

Drugs that would increase flow of bile were sought by ancient medical investigators. The term cholagogue which was used to designate drugs that increase the flow of bile came into use between the time of Hippocrates and Galen, but Galen made the term popular. From the time of Galen until the experimental work on the liver by Claude Bernard, medical men were content to use their so-called cholagogues and fallaciously to measure results obtained by changes in the color of the feces.

About the time modern research had shown that most of the so-called cholagogues were ineffectual in increasing the production of bile Brugsch and Horsters originated the term chol-

eretic to designate a drug which increases the flow of bile from the liver as distinguished from the term cholagogue which means expulsion of bile from the gallbladder.

Experiments on the content of bile began with the development of modern chemistry. In 1833, Demarçay separated three substances from bile which were probably bile acids. Ten years later (1843) Strecker isolated glycocholeic and taurocholic acid and showed their relation to cholic acid. From this time on chemists have been very active in this field of research. To illustrate, Vahlund received the Nobel prize last year for his work on the structure of cholic acid.

As soon as chemists began to isolate and prove relationships of the various compounds of the bile acids the pharmacologists began to administer these compounds to animals. It was soon found that bile acids and many of their compounds actually increased the flow of bile. In general, the administration of bile acids and their salts has been disappointing because they may be toxic. At the present time, however, there is a sodium salt of dehydrocholeic acid which is not toxic when given in doses of from

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0.5 to 2.0 gm (intravenously) This salt is prepared in aqueous solution, sterilized and put in ampules ready for use. It is sold under the trade name of "decholin."

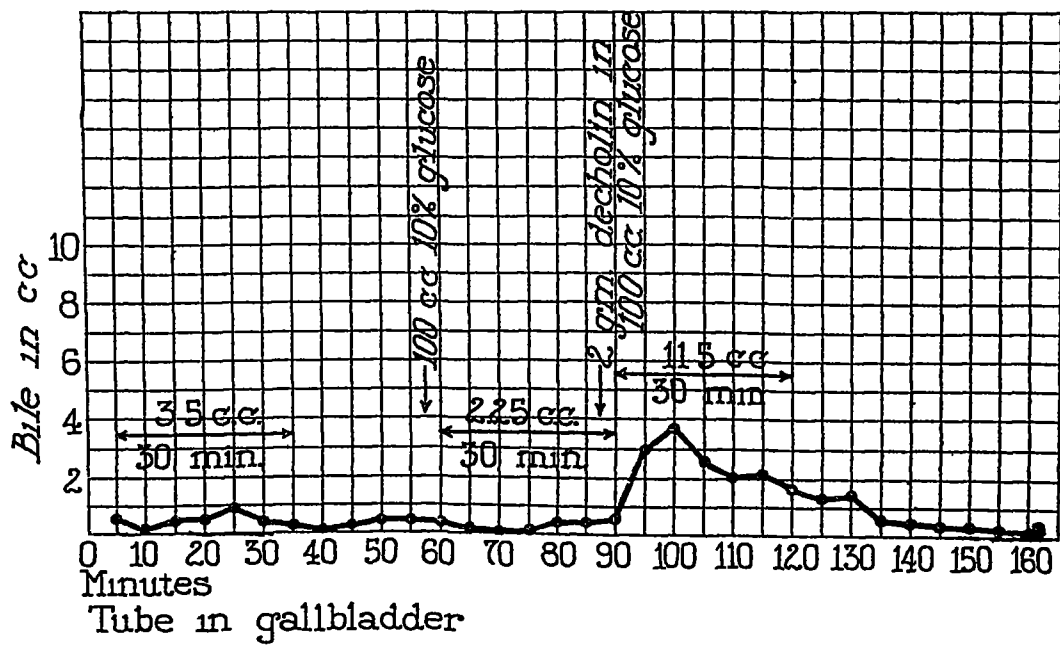
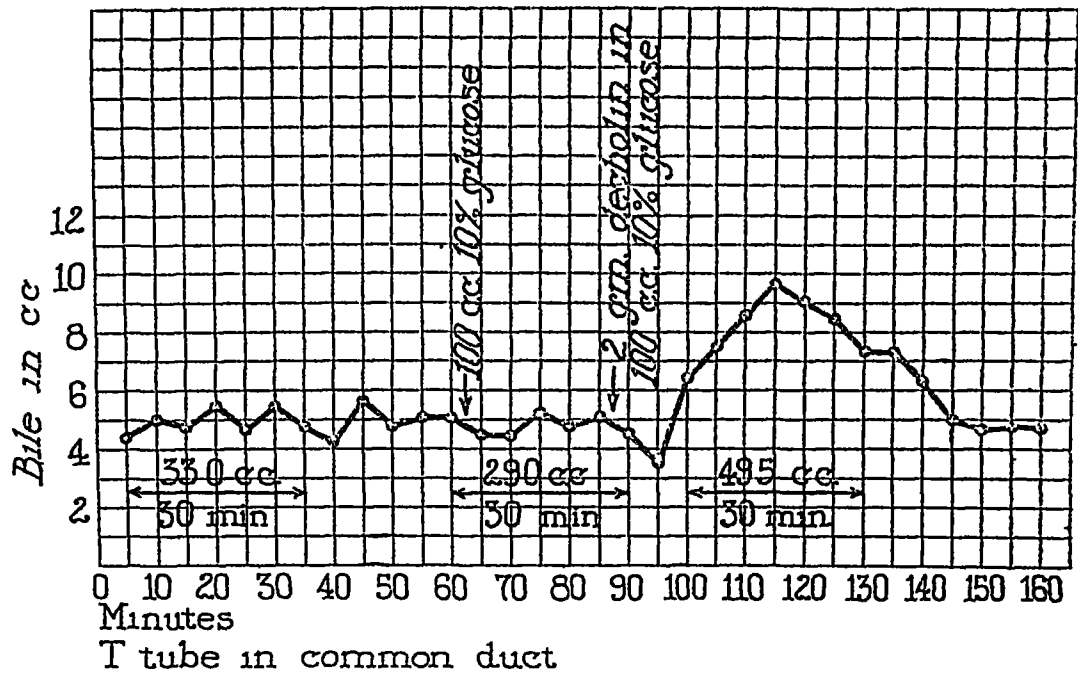
Our observations were made on three groups of patients. In the first group external biliary drainage had been established with a T-tube in the common bile-ducts with a tube to the outside. In the second group the tube in the gallbladder opened to the outside, in this group the common bile-duct was completely occluded by a pancreatic neoplasm. In the third group the patients had not been operated on and were selected after it had been shown that a free flow of bile could be obtained with a duodenal bucket and tube.

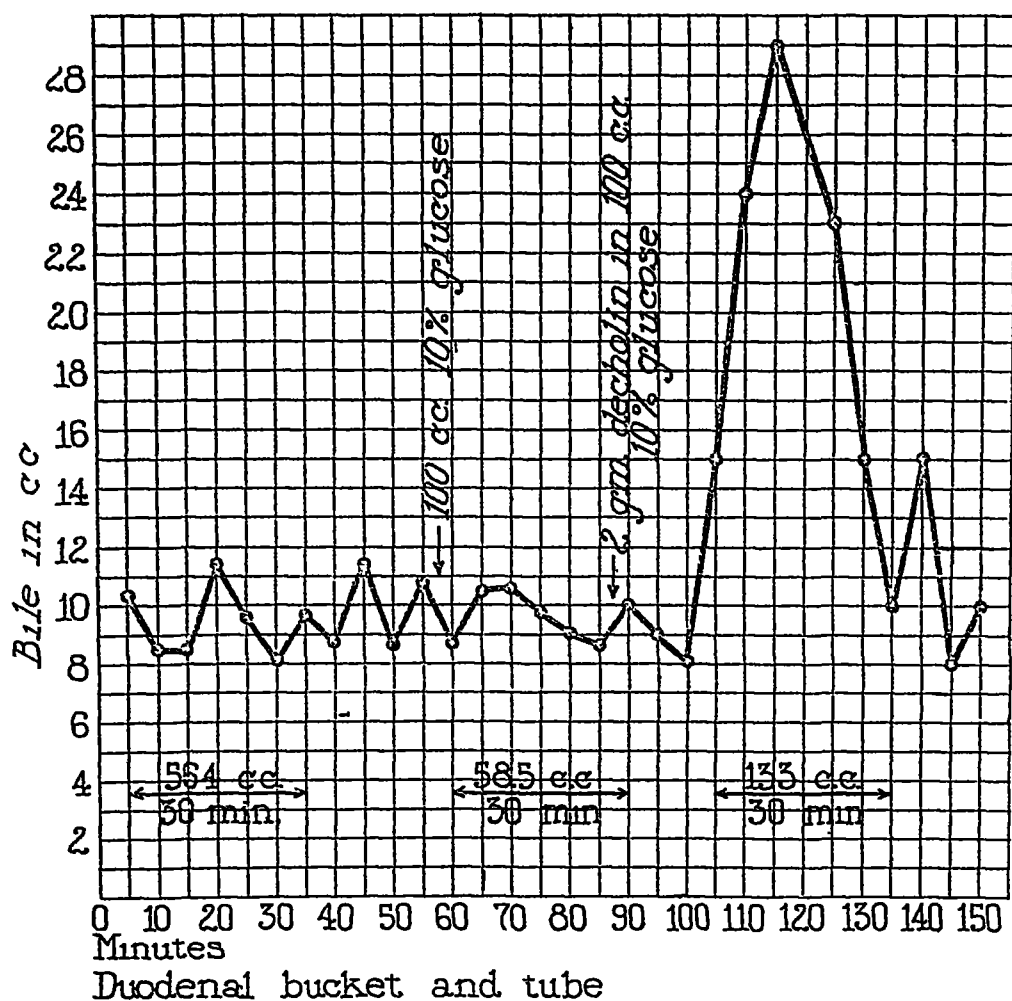
In a general analysis of the results it may be stated that all the experiments were begun about two hours after a meal, usually the noon meal. As far as possible a constant flow of bile was obtained. Frequently this took considerable time because patients with external bile drainage often had plugs of debris in the tubes which had to be removed by suction. In each experiment a period of one hour with an uninterrupted flow of bile was obtained before proceeding. This time is designated as the first control period. At the end of this period 100 cc of 10 per cent glucose was given intravenously. This was done to determine the effects on the flow of bile of giving 100 cc of fluids because we wanted to give the decholin diluted to a volume of 100 cc. Following the glucose the second control period was begun which lasted thirty minutes. At the end of this period the decholin diluted

to 100 cc with 10 per cent glucose was given.

The bile was collected in five-minute periods throughout all the experiments. During the experiments the patients remained quietly on the back or right side or in the same position during the entire time. That is, changes in the position were carefully guarded against.

In an analysis of the curves (figs 1, 2 and 3) certain definite points may be noted. The action of the drug is very prompt, in practically every instance the increase of the flow of bile was within fifteen minutes and in many instances the increase began much more promptly. The variations in the length of time before the increase in the flow of bile began cannot be attributed to the technic and time which it took to administer the drug. All the injections were made with size 18 needles and finished within a period of not more than five minutes. Some of the responses which were delayed more than ten minutes might have been due to plugs of debris in the tubes. At a casual glance one notices that there is a variation in the amount of increase in different patients (table 1). The peak of maximal response varies somewhat (figs 1, 2, and 3 and table 1). It is possible that some of the delayed maximal responses were also due to debris and mucous plugs in the tubes. In practically every instance of external biliary drainage during the time the flow of bile was increasing there was a constant shower of mucous plugs and debris. The increase in the flow of bile was usually over within an hour after administration.





In table 2 are shown some of the physical and chemical changes which take place in the bile. In order to make such studies it was necessary to pool the bile collected for ten or fifteen minutes before, during, and after the action of the drug in order to have sufficient quantities to work with. At the period of maximal choleresis the color of the bile was less intense. The bile salts, bilirubin and cholesterol were decreased relatively and absolutely. There was no definite change in the specific gravity. The dried weight increased.

It seems that the natural occurring constituents of the bile are diluted and at the same time the specific gravity is approximately maintained. The total solids are increased. Perhaps this can be accounted for by assuming that it is the decholin being excreted in the bile which keeps up the specific gravity. The values for the total solids are of little significance in a fluid which contains as much debris from tubes and varying amounts of mucus as bile.



TABLE I

COMPARISON OF VOLUMES OF BILE EXCRETED DURING THE FIRST AND SECOND CONTROL PERIODS AND DURING THE HEIGHT OF THE ACTION OF DECHOLIN\*

Cases	Bile at thirty-minute intervals, c c		
	First control period	Second control period	Height of action of decholin
	Tube in gallbladder		
1	85	90	185
2	280	270	490
3	30	15	160
4	170	220	580
	Tube in common bile-duct		
5	145	120	270
6	564	585	1330
7	440	585	1295
8	30	50	175
9	175	150	260
10	195	140	305
11	385	300	560
	Duodenal tube and bucket		
12	395	350	1200
13	210	255	410
14	130	100	805
15	300	400	750
16	105	100	95
17	85	70	80

\*Results shown in the curves are not included in this table

## COMMENT

We have not determined the normal choleretic action of decholin because a patient cannot be considered normal if it has been necessary to put a T-tube in the common bile-duct or a tube in the gallbladder. A duodenal tube and bucket is the only direct means of determining increase in the flow of bile in the normal person, and this is beset with uncontrollable errors. Some of the bile is swept away from the bucket and the bile collected is probably diluted with gastric and duodenal contents. Evidence of toxic effects were watched for and none was

observed, it should be noted, however, that in all of the patients employed there was a free flow of bile, either naturally or induced by artificial means\*.

\*McVicar intended to carry this work further. Since, by his death, he was prevented from publishing further reports, we append this note. In the course of work not connected with the present report, the drug was given to two subjects in whom the flow of bile was not free. In both, the concentration of serum bilirubin promptly rose. In one of them, who had a stone in the common duct, the injection was followed by pain.

TABLE 2  
CHANGES IN THE CHEMICAL AND PHYSICAL PROPERTIES OF THE BILE BEFORE,  
DURING AND AFTER THE ACTION OF DECHOLIN

	Color	Volume, c c	Bile salts, mg per cent	Bilirubin, mg per cent	Specific gravity	Dried weight, gm	Cholesterol		
							Bloor I	Bloor II	Split
Before	Dark amber	10	580.0	16.4	1.012 1.015 1.018	0.0573	65.0	69.0	4.0
During	Light amber	29	191.0	6.4	1.018 1.010 1.012	0.6120			
After	Amber	10	113.3	3.75	1.012 1.014 1.014	0.0208	30.0	30.0	

## SUMMARY

We have been able to repeat the work of various investigators on the choleric action of decholin. It has been found to be nontoxic in the doses given in patients in whom the flow of

bile was free. The change which takes place in the bile seems to be one of dilution of the normally occurring constituents. An increase in the flow of bile was obtained in eighteen of twenty cases.

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# Fatal Purpura Complicating Chronic Interstitial Nephritis\*

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**P**URPURA hemorrhagica is frequently accompanied by changes in the kidney and the suprarenal glands. The kidney may show evidences of hemorrhagic nephritis or only slight degenerative changes in the tubular epithelium with numerous foci of intertubular and intratubular hemorrhage. Little<sup>1</sup> cites four cases in infants and young children with hemorrhage into both suprarenal capsules proving rapidly fatal, and in which purpura was noted before death. At the post-mortem the chief finding was the hemorrhage into the capsules, the kidneys showing no changes beyond occasional hemorrhages. He also cites two very remarkable cases in which there was hemorrhage into both suprarenal capsules, not associated with other purpuric manifestations, and four cases of hemorrhage into one suprarenal capsule proving more or less rapidly fatal, but not associated with other purpuric manifestations.

Stevens and Peters<sup>2</sup> list a series of twenty-five cases of hematuria associated with clinical evidences of acute hemorrhagic nephritis. When it was possible to obtain the kidneys, they were found much enlarged and con-

gested. Minot<sup>3</sup> states that chronic nephritis, arterio-sclerosis, and the debility of old age may be accompanied by simple symptomatic purpura and very rarely by symptomatic purpura hemorrhagica. He further adds that the change which occurs in the blood of these patients with chronic nephritis which permits bleeding, is unknown, and that the platelet count and coagulation time are usually normal. He cites a case of purpura developing in a girl following an attack of scarlet fever at the age of eight. Chronic nephritis developed and during the last fifteen years of her life she had intermittent bleeding from the stomach, gums, nose, and uterus, death occurring at the age of forty-five from cerebral hemorrhage.

Silver<sup>4</sup> reported an interesting case of purpura occurring in a tailor aged 52, who from the age of 27 suffered with headache, nausea, vomiting and purpuric spots all over the body. At the autopsy, there were evidences of extravasations of blood into many organs, the spleen was small and shrunken, the liver cirrhotic and fatty, the right kidney contained a cyst about the size of a walnut in the upper pole and filled with bloody grumous fluid. The capsules of the kidneys were somewhat adherent, the surfaces of

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th organs were granular and the cortical portions pale. The weight of the kidneys was  $11\frac{1}{4}$  ounces.

The following case report is that of a patient seen for the first time two weeks before her death. The diagnosis of purpura had not previously been made. When first seen, she was sanguinated, delirious, and would readily lapse into a comatose state. The blood examinations showed the presence of secondary anemia and platelets were abundant in the smear. Four days after the first transfusion, the platelet count, the bleeding and agulation time were within normal limits. Duke<sup>5</sup> states that the life of platelets is but a few days, so that the above normal findings cannot be ascribed to the transfusion of 500 c.c. citrated blood. He noted that the platelets of normal individuals introduced into three patients having purpura hemorrhagica, disappeared within a period of about three days. Because of the blood examination, the diagnosis of simple symptomatic rather than hemorrhagic purpura was made. The patient was evidently suffering from uremic manifestations which are rare in true purpura hemorrhagica. Upon her admission to the hospital, twenty-five ounces of urine were obtained by catheter, but thereafter she voided from eight to twelve ounces during the day, as nearly as could be determined. The urine was pale, of low specific gravity and no casts were reported. Unfortunately, chemical examinations of the blood were not made. Considering the markedly contracted and sclerotic kidneys, which stripped of their fatty capsules weighed only 43 and 48 grams each,

or 91 grams together, the purpuric manifestations were considered as secondary to the interstitial nephritis, probably founded upon some infection suffered earlier in life.

*History of Case.* Mrs. H. B., a white woman, aged 37, gave a history of having felt weak and indisposed for the past year. She was able to get about until two weeks before her admission to the hospital, or four weeks before her death. She had suffered from chills and sweating spells during the past year and had lost one hundred pounds in weight. She had been able to eat all types of food, but had vomited frequently for the past six months, the vomitus consisted of a clear watery fluid and occurred every morning. The remainder of the day she usually felt well. There was no jaundice and no blood in the stools. Occasionally she experienced pain in the lower abdomen. The menstrual periods had always been regular until the past four or five months when she noticed at times that she would menstruate twice a month. At times she would flood profusely. The personal history was negative except for a previous appendectomy. She had two children living and well, one died at birth. Her husband was living and well, and gave no history of venereal disease.

For the past two weeks she suffered from increasing dyspnea, she had been coughing considerably. The feet had been swollen for the past two years. During the past few days she had been vomiting more frequently than before, at times the vomitus contained blood. About two years ago she urinated frequently at night, as

many as eight or ten times. She drank large quantities of water. The nocturia gradually disappeared and during the past week she did not have to get up to void. There were no changes in the bones or joints. She had constant headache with radiating pains in the spine. There was some visual disturbance, at times she had diplopia and again she would be scarcely able to see.

The patient was large, still quite obese, acutely ill, very dyspneic, temperature 99, pulse 90, respiration 24. The skin was dry, loose, and showed several large purpuric spots over the back and thighs and upper extremities. The nail beds and mucous membranes were markedly anemic. The pupils were small and reacted to light and accommodation. The sclerae were clear, the ears and nose apparently normal. The teeth were in fair condition, small petechiae on both cheeks. Slight bleeding from the gums, tongue coated, pharynx slightly injected and the tonsils not enlarged. The thyroid and cervical glands were not enlarged. The chest was well developed, respiration equal but somewhat shallow. Small râles were heard over both bases. The breasts were negative. The left border of the heart measured 11 cm to the left of the midsternal line in the fifth interspace. The sounds were somewhat distant but clear, there was a slight systolic murmur heard best over the apex and not transmitted. The pulse equal and regular, blood pressure 110 systolic, 60 diastolic. The examination of the abdomen was essentially negative. The extremities were negative except for slight edema in the lower and scattered purpuric

eruptions. The vaginal examination disclosed a bloody discharge from the uterus, the cervix was rather firm and showed an old laceration, but no ulcerations. The cul de sac and fornix were negative. The fundus of the uterus could not be felt.

Fluoroscopic examination of the chest showed the lungs to be clear, the heart slightly enlarged in the lower transverse diameter, the diaphragm normal in position, the costo-phrenic angles clear. The urine was straw colored, clear, sp gr 1.008, alkaline, albumin 0.4% of 1%, no sugar, the sediment contained ten white cells per field, no red cells, no acid fast organisms, quite a few streptococci, no casts were found. Before the transfusion, the blood examination showed hemoglobin 45 per cent, the red cells numbered 2,170,000, the white cells 18,050 of which 85 per cent were polynuclears and 15 per cent small lymphocytes. The red cells showed marked variation in size and outline. No nucleated red cells were found at the first examination, subsequently a few were found but no reticulocytes. Four days after the first transfusion of 500 cc of citrated blood, 240,000 blood platelets per cumm were found, the coagulation time was 3 minutes, and the bleeding time 5 minutes. The clot was not studied. The Wassermann reaction was negative. The sputum contained numerous fusiform bacilli, occasional spirochetes, a few streptococci and diplococci, but no acid fast organisms. Yeast cells were also present.

The treatment was of temporary benefit only. Following hypodermoclysis of salt solution, some fluids by mouth and transfusion of 500 cc of

blood, there was some improvement. The patient became more quiet, was able to talk rationally, and retained some food. Soon a swelling of the right parotid gland developed which yielded only a bloody secretion on incision. Her condition grew more serious, the restlessness and delirium returned with some stupor, severe hemorrhages from the rectum and vagina followed, and she failed to rally after a second transfusion. She died on March 20, 1929, just 13 days after admission to the hospital.

Autopsy performed soon after death by Dr. Joseph N. Ganim who was permitted to open the abdomen only. Protocol: Mrs. H. B., white woman, aged 37.

*External Examination* The body is that of a middle aged, slightly obese, fairly well developed white woman measuring 166 cms in length. The body surface is still warm and there is little apparent rigor mortis. The skin of the face is studded with a few discrete purplish pigmented areas covered with small crusts. Occurring rather infrequently on the thighs, arms and back are a few areas of pale, purplish ecchymoses. In addition the soft tissues of the right face along the angle of the mandible are swollen, somewhat indurated and of a purplish hue. A short wound one cm in length is present just above this angle of the jaw on the right side. The body surface is otherwise negative except for a healed right rectus scar. Pelvic examination reveals a marital outlet, edematous cervical lips, an oval, smooth uterus but no palpable appendages.

*Abdominal Cavity* The peritoneal

cavity contains a few c.c. of pale, straw colored fluid. The omentum is adherent along the old right rectus scar. The abdominal viscera reveal little of note on external inspection. Except for an absent appendix, the gastroenteric tract is not remarkable. It contains no free blood.

*Liver* The liver is normal in size. The capsule is smooth and the cut surface is pale, grayish-brown with fairly well preserved markings but increased friability. The gall bladder is not remarkable. The bile ducts are patent.

*Spleen* The spleen is not enlarged. The capsule is shaggy, as the result of fibrous adhesions. The cut surface is pale brick-red and well preserved with equal prominence of the connective tissue markings and Malpighian bodies. Friability is slightly increased. The internal genitalia are not remarkable.

*Kidneys* The adrenals are normal and well preserved. Both kidneys are infantile in size and nodular. The right measures  $8.5 \times 3 \times 1\frac{1}{2}$  cm. The respective weight of the kidneys is 43 and 48 gms. The nodular appearance is essentially in the parenchyma. This appears as cream colored, papillated tissue which in the cut surface closely resembles fat. The capsules strip with relative ease being only infrequently adherent. The cut surface is a combination of pink and gray hues. There is marked narrowing of the cortex and medulla. The markings are not recognizable. The ureters are patent and the urinary bladder, aside from being spacious is relatively normal.

*Heart* The pericardium and heart, aside from some increase in size of left ventricle and some dilatation of the right side, reveals little additional

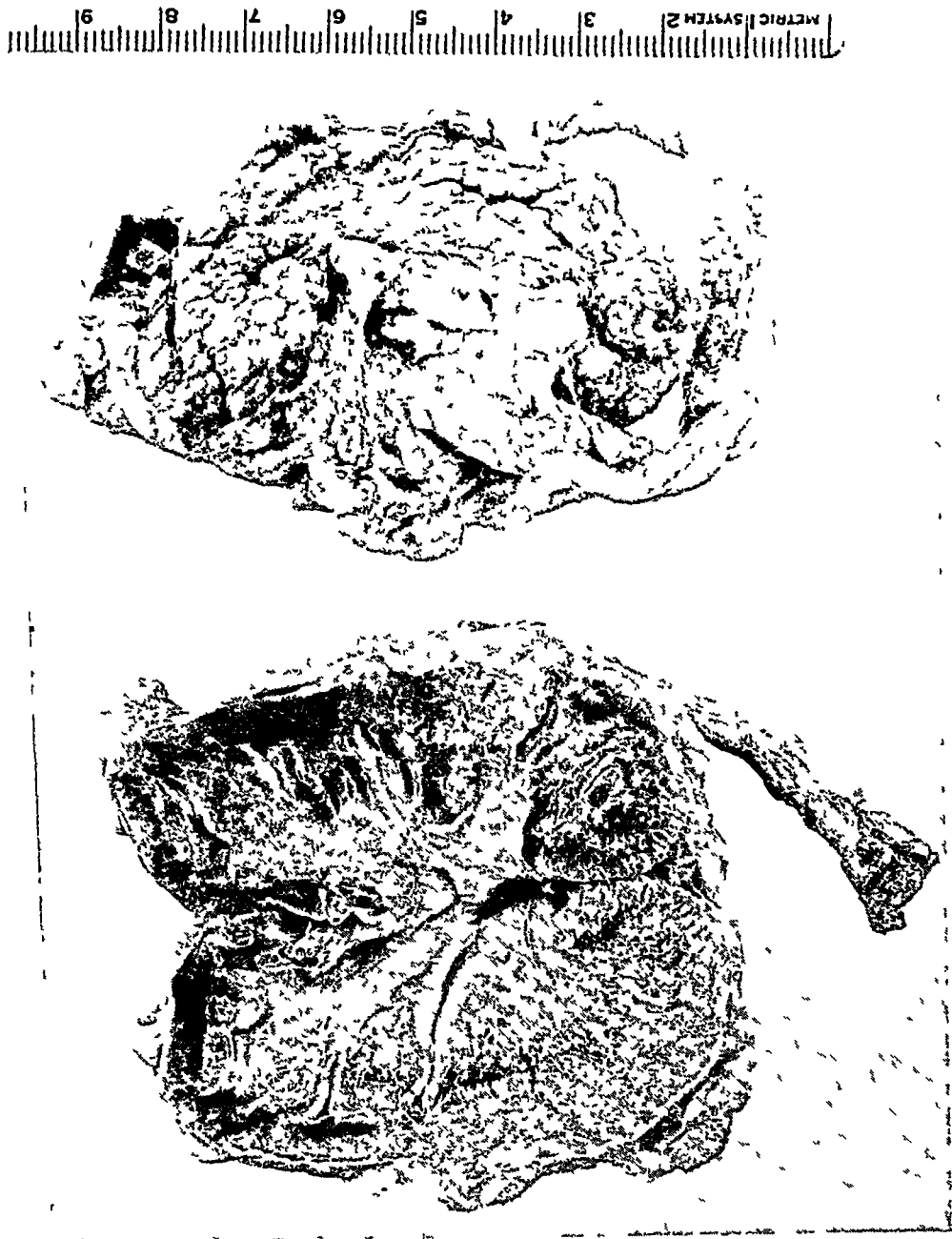


Fig 1 Kidneys weighing 48 and 43 grams respectively, marked narrowing of the cortex and medulla



Fig 2 Showing the dilated and distorted tubules, the sclerosis of the vessel walls, hypertrophy of the interstitial tissue, a large well preserved glomerulus with some sclerosis of the capsule M x 200





Fig 3 The same glomerulus magnified 800 times

pathologic changes The coronary arteries and aorta are not remarkable

*Lungs* The right lung, especially the lower lobe and to a lesser extent the left lung, present numerous patches and confluent areas of small, moderately deep red pneumonic infiltrations varying from friable to relatively firm tissue Only a few fibrous pleural adhesions are found on the right side The tracheo-bronchial mucous membrane and corresponding lymph-nodes are not remarkable

#### MICROSCOPIC EXAMINATION

*Kidney* Renal capsule not present in section except for occasional small adherent thickened strip Many glomeruli are sclerosed while others show thickening of capsule The better preserved glomeruli show no appreciable increase or reduction of nuclei or tufts The blood vessels especially the small show definite sclerosis most apparent in the intima Most of the tubules are dilated and distorted, the lining epithelium is flattened and in some instances lay loose in the lumen The lumina contain moderately pale pink hyalin-like bodies The interstitial connective tissue is relatively increased and contains a goodly number of lymphocytes The pelvis presents an intact mucous membrane and submucosa contains numerous lymphocytes and a few endothelial leucocytes

*Spleen* Capsule slightly thickened, lymphoid elements quantitatively reduced, framework is prominent, hyaline changes in thickened vessel walls

*Heart* Not remarkable

*Cervix* Dilated gland with epithelial hyperplasia of (glandular) cells, submucosa contains moderate number of lymphocytes

#### Anatomical Diagnosis

- 1 Chronic interstitial nephritis
- 2 Active nontuberculous pyogenic lobular pneumonia
- 3 Acute parotiditis
- 4 Petechial hemorrhages and ecchymoses into skin
- 5 Laparotomy scar

#### Microscopic

- 1 Chronic interstitial nephritis (contracted kidney)
- 2 Chronic fibrous splenitis
- 3 Chronic cervicitis

#### SUMMARY

In a woman aged 37 death occurred as a result of simple symptomatic purpura and uremia, the autopsy disclosed the presence of markedly contracted kidneys weighing only 91 grams The blood platelet count, the bleeding and clotting time were within normal limits Renal complications had been present over a period of two years, but the purpuric symptoms had been either overlooked or manifested themselves only by increased menstrual flow, until a short time before her death

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- <sup>2</sup>STEVENS, A R and PETERS, J P, Jr Urinary Tract Purpura, A Probable Entity, Journal of Urology, Baltimore Vol IV, Feb, 1920, pp 1-97
- <sup>3</sup>Nelson's Loose leaf Medicine, Vol IV, Chapter III, pp 128 and Chapter VI, pp 159
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- <sup>5</sup>DUKE, W W Journal Exp Med 1911, Vol XIV, pp 265 and J A M A 1910, Vol LV, pp 1185

# A New Case of Syphilitic Tumor of the Stomach Cured by Antiluetic Treatment

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THE older literature on syphilis of the stomach can be found in the papers of LeWald,<sup>1</sup> Eusterman,<sup>2</sup> and myself<sup>3</sup>

A recent paper on syphilis of the stomach by Singer and Meyer<sup>4</sup> is of great interest in showing that cases of syphilis of the stomach most probably heal perfectly during life. The authors arrive at this conclusion from the following facts. In a period of six years these eminent surgeons found microscopic evidences of syphilis merely in four surgically resected parts of the stomach. During the same length of time not a single instance of gastric syphilis was encountered by them in five thousand autopsies. The authors assume that retrogression of the syphilitic infection in the stomach frequently occurs.

Whether this healing process takes place without any further medication or merely by the well known antiluetic remedies, is difficult to say. This, however, refers to the smaller lesions (ulcers, erosions, gastritis) but not to tumors of the stomach of a luetic nature.

The latter group appears but rarely, resembles real neoplasms so much, that it is usually taken for cancer, and is frequently accompanied by a fatal issue. This group is therefore of the

greatest importance and I take pleasure in discussing this subject before you. In my practice I have seen altogether ten cases of syphilitic tumors of the stomach of which I have described seven in different papers.\* Of the three more recent cases I shall report one, the last one observed. The case is as follows.

Herman S., 45 years old—Salesman. Sept 25th, 1928.

Previous history. Never ill before, never operated upon.

Married 18 years, no children, wife was told she must be operated upon for sterility.

Patient denies venereal disease.

Present trouble started in March, 1928, with marked constipation. Appetite became poor. Bowels did not move in two or three days, whereas formerly they were always regular. Patient consulted his family physician who gave him some medicine and he felt better for three months. Then in May, 1928, patient complained of cramps in the legs and began to feel dizzy. Appetite became poor again but improved after taking some medicine. Patient then felt good for one month. In June patient noticed that he was becoming pale and losing weight. He had X-ray pictures taken of his gastrointestinal tract and was told he must undergo an operation at once. He lost about

\*Remark 2, in my paper, Syphilis of the Stomach. Philad. Medical Journal, Feb 3, 1900, 1, Journal of the American Medical Association, Oct 25, 1902, 1, International Journal of Surgery, Jan, 1909, 3, Medical Record, March 13, 1915.

15-18 pounds from March until September 25, 1928, at which time he consulted me.

Chief complaints Dizziness, loss of weight, weakness, loss of appetite, and pains in the legs. Patient looked pale and became exhausted on slight exertion.

Physical examination of the abdomen revealed a resistant mass of walnut size to the left of the median line but near it under the costal margin. The liver was slightly enlarged but not indurated.

The gastric contents examined one hour after Ewald Boas test breakfast showed  $\text{HCL}=\text{O}$ , reaction hardly acid.

The gastric contents were again examined on Oct 2nd with a similar result  $\text{HCL}=\text{trace}$ , Acidity=10. The string test was negative. Wasserman++++.

A diagnosis of a probable syphilitic tumor of the stomach was made and patient put tentatively on an antisyphilitic treatment (Salvarsan and Iodides). Patient began to improve pretty soon after this regime. On Nov 8th the resistance was still there but only a trace of it palpable. Patient felt stronger and reported a gain of eight pounds. On January 9, 1929, patient felt well and there was no resistance palpable in the gastric region. He continued to gain in strength and health. Beginning of February, 1929, patient showed a gain in weight of 30 pounds and his Wasserman became negative. It was of great interest to control the result of treatment with X-ray pictures taken at different times and to ascertain whether we could find a change in the anatomical state of the stomach. We give therefore the roentgenograms taken before and after treatment.

The interest this case presents lies in the fact,—that to all appearances patient seemed at first hand to be troubled with malignant neoplasm of

the stomach. We had here a comparatively short history of disease, a palpable tumor, absence of hydrochloric acid in the gastric secretion, and a pronounced gastric defect by the X-rays. With all these pathognomonic signs there were present loss in weight and strength and severe dyspeptic symptoms. The presence of the Wasserman reaction (++++) gave a clue to the possibility of having to deal here with a gummatous tumor of the stomach. The course of the disease, its complete response to the instituted antiluetic treatment, and the disappearance of the Wasserman reaction after the cure, show that syphilis of the stomach was the only affection here present. This finds confirmation in the X-ray pictures which show a gradual recession of the tumor and return of the stomach to its normal configuration.

I take pleasure in thanking my associate Dr H A Rafsky for the X-ray pictures and his assistance in the treatment of the case.

<sup>1</sup>DOWNES, W A, and LEWALD. Journal American Medical Association, May 29, 1915, page 1824.

<sup>2</sup>EUSTERMAN. American Journal Medical Sciences, Jan 1917.

<sup>3</sup>EINHORN, MAX. Philad Medical Journal, Feb 3, 1900.

<sup>4</sup>SINGER, H A, and MEYER, K A, Chicago. Syphilis of the Stomach, Incidence. Surgery, Gynecology, Obstetrics, Jan, 1929. 48 1-144.



FIG 1 Roentgenogram of stomach of Herman S on Sept 19th, 1928 before treatment. A big defect is visible involving the antrum pylori and portion of stomach adjacent to it.

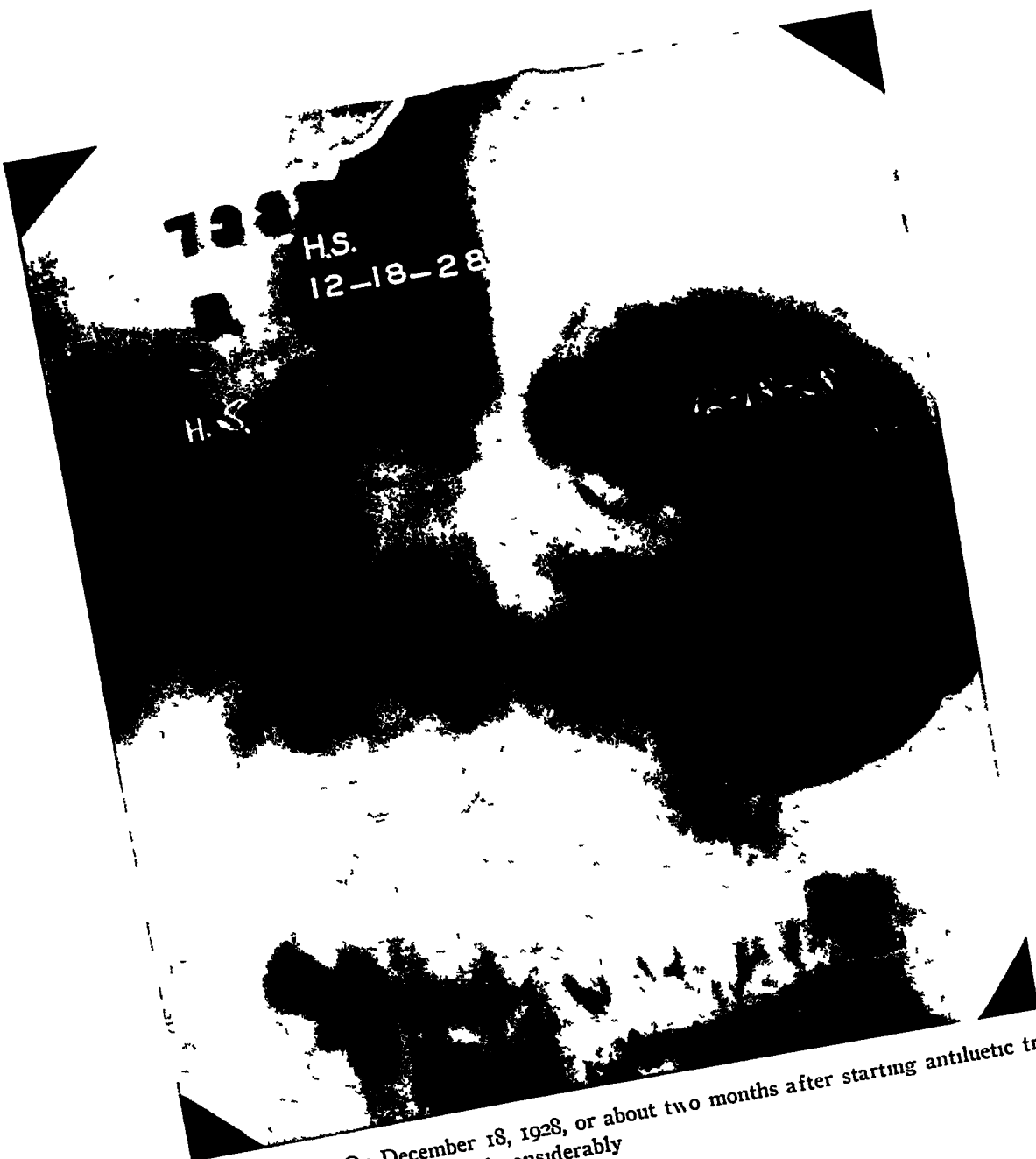


FIG 2 Do On December 18, 1928, or about two months after starting antiluetic treatment The defect has decreased considerably

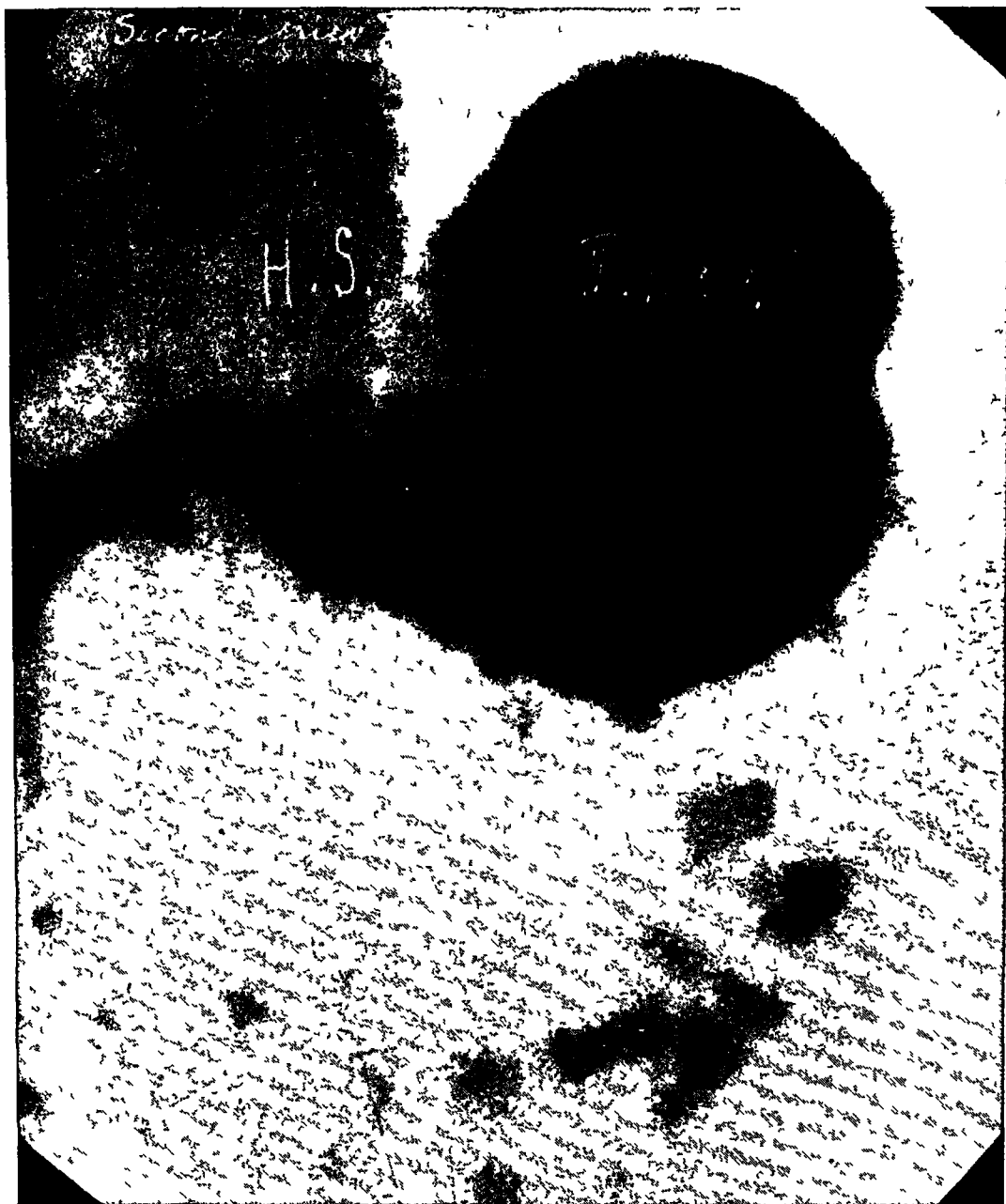


FIG 3 Do February 1, 1929 The antrum and pars pylorica show up more favorably  
The defect has almost disappeared

# The Treatment of Urticaria and Angioneurotic Edema\*

By GRANTON TYLER BROWN, B S, M D, F A C P, *Washington, D C*

URTICARIA and angioneurotic edema are commonly spoken of by the laity as hives and giant hives respectively. They are of frequent occurrence, and present to the physician one of his most difficult therapeutic problems.

This paper is based upon a careful study of a series of 160 patients with urticaria or angioneurotic edema. As the treatment of these two disease states is the same, I will deal with them together.

## ALLERGIC RELATIONSHIP

Urticaria belongs to the group of allergic diseases which includes bronchial asthma, hay-fever, and eczema. There is a close relationship between urticaria or angioneurotic edema, bronchial asthma, and hay-fever, as evidenced by the following facts. In some persons, their asthmatic or hay-fever attacks are initiated or accompanied by urticaria. Some individuals with urticaria or angioneurotic edema have definite asthmatic symptoms with their urticarial attacks and at no other time, which seem to be due to edema within the bronchial tubes. For example

One young woman with chronic urticaria, stated that she occasionally felt as if the hives broke out in her bronchial tubes, causing shortness of breath, and a wheezing sound which could be heard by others.

A woman with angioneurotic edema, stated that with her attacks of swelling, she had wheezing sounds in her chest.

Constitutional reactions from injections of extracts of foods, animal epidermals, pollens, etc., are frequently manifested by a combination of urticaria, angioneurotic edema, hay-fever, and asthma. Such constitutional reactions, as well as the urticaria of serum sickness, are best treated by epinephrine or ephedrine.

## HISTORY TAKING

The curative treatment of urticaria is, in most cases, based upon a specific diagnosis, and an exhaustive history is of fundamental importance in arriving at such a diagnosis. In other words, by careful questioning alone, the causative factors can frequently be elicited. The method of taking a complete history in urticaria is the same as in bronchial asthma, which has been fully dealt with in a preceding article.<sup>1</sup> I will give some illustrative excerpts from case histories.

\*Read at the 30th Annual Meeting of the American Therapeutic Society, Pittsburgh, Pa., April 6, 1929.



A boy of 10 years was brought to me with angioneurotic edema. His parents stated that when he was 6 years old, eating eggs caused his first attack, in which his ears were swollen, nose distorted, and all of his features changed. They also stated that eating certain kinds of nuts, especially English walnuts, affected his mouth, made his throat itch, and upset his stomach. Almonds and peanuts did not seem to bother him. Peanuts, of course, are not nuts at all, but belong to the legumes. After petting a dog, his hands would itch. On cutaneous tests, he gave an enormous reaction to English walnut protein, marked reactions to egg yolk, ovomucoid and black walnut, and a moderate reaction to dog hair. Almond was negative, and peanut gave a slight or doubtful reaction.

A man of 50 with hives, stated that drinking grape juice caused them. He gave a marked positive reaction to a skin test with grape protein.

A 7 year old boy had hives within a few minutes, every time he ate eggs, and they were the only food that his parents had noticed would cause them. Out of 48 skin tests, his only positive reactions were to the different proteins of egg.

A young man of 18 said that eating buckwheat made him break out in hives. He gave a marked positive skin reaction to buckwheat protein.

A girl of 10 years was brought to me with urticaria. Her mother stated that milk disagreed with the child, and always caused red blotches around her mouth and generalized hives. She never used to vomit milk, but recently had been unable to retain it. On tests, the child reacted markedly to the

protein of whole milk, and also to the casein and lactalbumin fractions.

A woman of 35 had angioneurotic edema. The attacks made her lips and tongue swell. There was an itching way in the back part of the roof of her mouth, and an itching deep in her ears, so that she felt as if she wanted to dig them out. There was also an itching and swelling in her throat, and her esophagus seemed tight. She gave as causes, bananas, tomatoes, celery, nuts, watermelon, grapes, figs, dates, and onions. All of the foods named gave positive reactions, with the exception of watermelon, figs, and dates, which were not tested.

A man, aged 31, had noticed for the preceding 9 years that eating cantaloupe or bananas would produce hives, and spinach would cause his tongue to break out in welts. A physician who would not believe that so healthful a food as spinach could harm anyone, gave him a hypodermic injection of the juice from cooked spinach, and it made him unconscious for two hours. He reacted to cutaneous tests with cantaloupe, banana, and spinach.

A woman, 32 years of age, stated that eating grapefruit caused severe urticaria, and cantaloupe made her throat itch. She gave a marked skin reaction to grapefruit protein, and a moderate reaction to cantaloupe.

People with urticaria are, of course, frequently suspicious of certain foods that have nothing whatever to do with their trouble. On the other hand, the failure to obtain a positive reaction to a skin test with the protein of some particular food is not sufficient to rule out that food as a cause.

## SKIN TESTS

Positive reactions to skin tests are relatively infrequent in urticaria, in comparison with bronchial asthma. Someone has attempted to explain this discrepancy by stating that the urticarial reaction takes place in the blood vessels of the skin rather than in the skin cells.

As a positive reaction to a skin test is manifested by an urticarial wheal, one would think that skin tests would diagnose practically all cases of urticaria, but unfortunately they will not. For example, I have had two severe attacks of acute urticaria from eating too many tomatoes, and yet when I am tested with tomato protein that I know to be potent, I give absolutely no reaction to it. Therefore, when patients with urticaria are suspicious of certain foods that fail to give positive skin reactions, these foods should be completely eliminated from their diet for a sufficient length of time to prove their guilt or innocence.

Protein skin tests were made on 148 of the 160 patients with urticaria or angioneurotic edema in this series, and 60 per cent of those tested were found to be protein sensitive and 40 per cent negative. Sixty per cent sensitive, however, is too high a proportion for urticaria, as, in a number of the patients, the positive skin reactions were due to a concomitant asthma, hay-fever, or eczema.

**False Reactions** In testing patients with irritable skin or dermatographia, extreme care should be taken not to traumatize the skin any more than is absolutely necessary, and, to rule out false reactions, the tests should be interpreted in comparison with normal controls.

**Doubtful Reactions** Even slight or doubtful reactions to skin tests are worthy of consideration, as evidenced by the following case reports.

A man of 51 consulted me in 1925, with urticarial attacks that he had been troubled with for the preceding 20 years. All of his skin tests were completely negative, with the exception of doubtful reactions to spinach and celery. These foods were eliminated from his diet, and he has been entirely free of urticaria ever since, a period of nearly four years.

A man, aged 55, was referred to me with angioneurotic edema of two years duration. The swelling always affected one side of his face and head. He gave slight reactions to the proteins of cows' milk. Milk was completely eliminated from his diet, and when last heard from, he was entirely well of his trouble.

In eliminating from the diet such foods as eggs, milk, or wheat flour, it is, of course, necessary to eliminate all other articles that contain them.

**Delayed Reactions** Reactions to skin tests with food proteins almost always appear within five to thirty minutes. Occasionally, however, food reactions are delayed, and do not appear until some hours after the tests are applied. Therefore, if there are no immediate reactions, the sites of the tests should be examined at intervals during the succeeding 24 hours for the detection of delayed reactions.

## FOOD ADDITION METHOD

Even though the history and skin tests are negative, a diagnosis may be made at times by means of the food addition method, originally advocated by O. H. Brown.<sup>2</sup> The patient is put

on an exclusive milk diet for about a week, and if the urticaria clears up, it proves the cause to be some food or foods other than milk. Other foods are then added to the diet, one at a time every few days, and the reappearance of the urticaria carefully watched for. In this way, the offending food or foods may be detected. If the urticaria does not clear up after about a week of an exclusive milk diet, a diet of all kinds of food except milk and milk products is substituted. If the urticaria disappears on such a diet, milk is proved to be the cause.

#### NON-FOOD SENSITIZATION

Although foods are by far the commonest cause, urticaria may also be due to sensitization to animal epidermals, bacteria, pollens, drugs, etc. I will cite a few cases.

A girl, 2½ years old, was brought to me with asthma and urticaria. The first attack occurred when her father put her on a horse. Her eyes got red, she began to wheeze, and broke out all over in hives. She reacted, of course, to a skin test with horse dander protein.

A woman of 32 was recently referred to me with bad urticaria of four or five years duration. It affected her face, neck, chest, back, and arms, and occurred at all seasons of the year. The urticarial eruption was accompanied by terrible itching, and would last anywhere from a few hours to a day, and then disappear, only to promptly recur. She had tried, without results, various diets and medicines that had been prescribed for her. Skin tests were all negative. Cultures of her stool showed streptococcus hemolyticus in large numbers, and an

autogenous vaccine was prepared from this organism. When tested intradermally with the streptococcus hemolyticus vaccine, she gave a marked positive reaction. She was given injections of this vaccine at weekly intervals, in gradually increasing doses. Her urticaria promptly disappeared under treatment. It is interesting to note that following several of the increases in vaccine dosage, she had a transitory recurrence of the urticarial eruption.

A man was referred to me in 1924 with urticaria and dermatitis. He felt sure that his skin trouble was due to acid foods, and he named a long list of them that he could not eat. His attacks started the latter part of May and lasted throughout the summer. He had never had the least bit of this trouble in the winter. All food tests were completely negative, but he gave definite positive reactions to the pollens of the common grasses. In the spring of 1925, I gave him 16 rapidly increasing doses of grass pollen extract, and, in spite of eating whatever he pleased, he went through that summer without a sign of urticaria or dermatitis. I retested him in the spring of 1926, and he gave only very slight or doubtful reactions to the same grass pollens that he had been definitely sensitive to before treatment. He has had no treatment since, and there has been no recurrence of either urticaria or dermatitis.

A physician consulted me recently, with generalized urticaria that he had been troubled with almost constantly for the preceding seven months. As his urticaria began during the strawberry season, he thought at first that

they might be the cause, and had since been suspicious of eggs, wheat flour, and cheese. He had been under the care of a gastro-enterologist, and also a dermatologist, without results. On skin tests, he did not react to egg proteins, but did react to the proteins of wheat flour, strawberry, cheese, and a number of other foods. As he was using a dentrifice containing ipecac, I tested him cutaneously with powdered ipecac, and he gave one of his largest reactions to this substance. He was advised, of course, to eliminate from his diet all the foods to which he had reacted, and also to change his dentrifice. As a result, his urticaria cleared up. He had another acute attack of urticaria, however, after taking a small dose of cough medicine which he afterwards found contained ipecac.

Urticaria from ipecac sensitization is somewhat unusual. Peshkin,<sup>3</sup> and others<sup>4</sup> have called attention to the importance of ipecac sensitization as a cause of bronchial asthma in pharmacists, from inhalation of the drug in the preparation of Dover's powder. Peshkin also refers to urticaria of the hands and forearms from contact with emetin solution.

Quinine and acetyl-salicylic acid are the commonest drugs to cause urticaria. As Cooke<sup>5</sup> has already stated, drug sensitive individuals rarely give positive skin reactions to the offending drug.

#### NON-SPECIFIC FACTORS

People with urticaria not infrequently state that their attacks are brought on or aggravated by one or more of the following: getting overheated, hot baths, nervousness, excitement, hurrying, alcoholic drinks, emotional strain,

strenuous exercise, etc. These various influences all tend to cause an increased supply of blood to the skin, thus probably bringing more of the toxic substance to the skin capillaries. Patients should be advised to avoid, as far as possible, all such aggravating influences. Rough woolen clothing may be quite irritating, even to persons not sensitive to wool, and therefore should not be worn next to the skin.

#### NON-ALLERGIC STUDY

In addition to an exhaustive history and all necessary skin tests, the successful treatment of chronic urticaria and angioneurotic edema frequently depends upon a careful study of the patient as a whole. Such a study, in addition to a general physical examination, may include urinalyses, blood tests, determination of the basal metabolic rate, stool examination, bacteriological examinations, X-rays, etc. I will outline the general management of these cases, recommending somewhat didactically, those therapeutic measures that have seemed to give the best results.

*Urinalysis.* If the urine is too concentrated, namely if the specific gravity is too high, the patient should be advised to drink more water. If the urine is too strongly acid, the diet should be regulated to contain more of the alkaline foods, and less of the acid-forming ones. A teaspoonful of sodium bicarbonate in water, should be taken daily until the urine is alkaline. The litmus paper test is sufficiently accurate for determining the reaction of the fresh urine. The presence of albumin and casts indicates either a nephritis or a nephrosis, and calls for

further study, including a diligent search for some focal infection, and possibly a kidney function test, and blood chemistry. The detection of sugar in the urine calls for a blood sugar determination. A large amount of indican in the urine is strongly suggestive of intestinal putrefaction. Any tendency to constipation should be corrected by regulation of the diet, and administration of the simpler remedies, such as mineral oil, either plain or combined with agar-agar. Pus in the urine indicates infection somewhere in the urinary tract, and its source should be determined and properly treated.

*Blood Examination* Red, white, and differential counts, and hemoglobin estimations, frequently give helpful information. A low red cell count, namely an oligocythemia, calls for arsenic, which may be conveniently administered in the form of liquor potassii arsenitis (Fowler's solution), starting with one drop in a little water, three times a day after meals, and increasing one drop daily until five or seven drops, then decreasing one drop a day until one, then stopping a week, and repeating. A decreased percentage of hemoglobin, namely an oligochromemia, calls for iron, which may be given in the form of subcutaneous injections of the green citrate,  $\frac{3}{4}$  grain every three or four days, or iron may be given orally in 5 grain sugar-coated pills of ferrous carbonate, one or two pills to be taken three times a day after meals. In all cases of secondary anemia, a proper diet and generous doses of sunshine and fresh air should be prescribed. Leucocytosis and a relative increase of the polymorphonuclear

neutrophiles is indicative of focal infection. A blood eosinophilia is suggestive, but not diagnostic of protein sensitization. The subject of eosinophilia in allergy has been dealt with in another article.<sup>6</sup>

*Blood Calcium* The most valuable blood test that can be made in urticaria, is the determination of the ionic calcium. In a preceding paper on calcium deficiency,<sup>7</sup> the importance of standardizing the laboratory technic of calcium determination, and of establishing a definite calcium norm, has been emphasized. We have established for our laboratory technic 9.5 to 11 mgm per 100 cc, as normal calcium limits. Ten milligrams per 100 cc is average normal, and readings from 9.5 to 10 mgm not inclusive, are considered low normal.

We found that 42 per cent of patients with bronchial asthma, 40 per cent of patients with eczema, 37 per cent of those with perennial hay-fever, and 28 per cent with seasonal hay-fever, had a definite calcium deficiency. Calcium determinations were done on 60 of the present series of 160 patients with urticaria or angioneurotic edema. Fifty-eight per cent had a definite calcium deficiency, and 23 per cent were low normal. Therefore, calcium deficiency is much more frequently encountered in urticaria and angioneurotic edema, than it is in asthma, eczema, or hay-fever.

*Calcium Therapy* Patients with a low normal calcium should be given calcium lactate and parathyroid orally, and those with a definite calcium deficiency should be given the same, with the addition of air-cooled quartz lamp treatments.

According to the work of Roe and Kahn,<sup>8</sup> the optimum oral dose of calcium lactate is 5 grams, taken on an empty stomach. It has been found convenient to have the calcium lactate powder dispensed in a four-ounce glass jar, the screw cap of which level full holds 5 grams of the powder. The patient is instructed to pour a level capful of the powder on the surface of a glass of water, to wait until the powder all settles to the bottom of the glass, then to stir it up well and drink rapidly, following with a little clear water. This dose is to be taken twice daily, about one-half to one hour before breakfast and dinner, or the second dose may be taken at bedtime. Children are given 25 grains of the calcium lactate powder three times a day, one-half to one hour before meals. A half-ounce glass vial, the screw cap of which level full holds 25 grains of the powder, is supplied for measuring the doses.

For the occasional patient who cannot take the calcium lactate powder, 5 grain tablets of calcium lactate should be prescribed, one or two tablets to be taken three times a day, one-half to one hour before meals.

If it is desired to administer calcium intravenously, a sterile 10 per cent solution of calcium chloride should be used. The dose is from 2½ to 5 c c, and may be given two or three times a week. The solution should be injected very slowly into the blood stream, and, as it is extremely irritating to the tissues, great care should be exercised to prevent any from escaping outside of the vein.

The dose of desiccated parathyroid is 1/10 grain for adults and 1/20 grain

for children, prescribed in tablet form, to be taken three times a day, one-half to one hour before meals.

The mercury-vapor ultraviolet light treatments should be started with the quartz burner about 24 inches from the patient's body, for one or two minutes lying face down, and then for the same time lying face up. For subsequent treatments, the time should be increased by one or more minutes (depending upon the amount of skin reaction from the preceding treatment), until a duration of twenty to thirty minutes both back and front, forty to sixty minutes in all, is reached. Then holding the time constant, namely, twenty to thirty minutes each way, the lamp should be lowered 1½ to 3 inches at a treatment (depending upon reaction), until the burner is about 12 inches from the patient's body. In other words, the treatments should be so regulated that the patient will have a mild skin reaction following each exposure. These treatments should be given every 3 or 4 days. Amber goggles should be worn to protect the eyes. An interval timer should be used for timing the exposures.

Those patients who, for one reason or another, cannot take the ultraviolet light treatments, should be given cod liver oil in teaspoonful doses three times a day.

Other than calcium determination, additional blood chemistry, such as blood sugar or uric acid, should be done whenever there seems to be any indication.

*Wassermann* Hazen<sup>9</sup> has mentioned syphilis as one of the causes of chronic urticaria. Wassermann and Kahn pre-

precipitin tests were done on 24 of my 160 patients with urticaria or angioneurotic edema, and they were all completely negative. It would seem that in urticaria, Wassermann or Kahn precipitin tests are indicated only where there is a history suggestive of lues, such as repeated miscarriages, frequent sore throat, etc

*Basal Metabolism* The basal metabolic rate should be determined on all patients who have symptoms of either hypo- or hyperthyroidism. For the metabolism test to be of any value, it is essential that the patient be basal at the time of the test. Rates from minus 10 to plus 15 are within normal limits. The basal metabolic rate was determined on 23 of the patients with urticaria or angioneurotic edema in this series, and of these, 8 were "hypo," 4 were "hyper," and 11 were normal.

Patients with a low metabolic rate should be given desiccated thyroid, which may be conveniently administered in tablet form. The dose is from 1/10 to 1 grain, three times a day, one-half to one hour before meals. It is preferable to start with 1/10 grain and then gradually increase the dose until the metabolism is brought to normal. The best single guide in thyroid dosage is the pulse rate.

Hyperthyroid patients should be instructed to take an abundance of rest, and all foci of infection, such as abscessed teeth or diseased tonsils, should be surgically removed. If the hyperthyroidism does not respond to rest and the removal of focal infection, X-ray treatment of the thyroid gland should be instituted.

One of the most intractable cases of

chronic urticaria that I have seen, was that of a young woman with hyperthyroidism. Her basal metabolic rate was plus 33, and as she refused to rest, she was referred to a radiologist for X-ray treatment of the thyroid gland. After several treatments, her urticaria disappeared. When I last heard from her, however, she had discontinued her treatments, and there had been a recurrence of the urticaria.

*Other Gland Therapy* Desiccated whole ovary or corpus luteum should be prescribed when there are symptoms of ovarian hypofunction, such as amenorrhea, irregular or scanty menstruation, or premature menopause (artificial or natural). The dose of either whole ovary or corpus luteum is five grains three times a day, one-half to one hour before meals. They may be conveniently administered in tablet form.

Desiccated whole suprarenal gland, one or two grains in tablet form, three times a day, one-half to one hour before meals, is worthy of trial in those patients with a definitely low blood pressure.

In urticaria due to food sensitization, pancreatin may prove helpful in promoting complete intestinal digestion of the various foods. Pancreatin should be prescribed in the form of 5 grain tablets with an enteric coating, so that they will pass through the stomach unchanged, as suggested by Sansum<sup>10</sup>. One or two of these tablets, usually the latter, should be taken after each meal.

*Stool Examination* The stools should be carefully examined for the presence of parasites or ova, excessive putrefaction, or abnormal flora such

as streptococcus hemolyticus. Patients with excessive intestinal putrefaction or abnormal flora, should be given a saline, such as sodium phosphate, every morning upon arising, for about a week, to thoroughly clean out the intestinal tract. This should be followed by fresh acidophilus milk, one quart daily, in divided doses. Patients should be advised to add a teaspoonful of milk sugar (lactose) to each glass of the acidophilus milk. The eating of the dextrin-containing fruits, such as figs, dates, raisins, or prunes, should be encouraged as an aid to acidophilus therapy.

If fresh acidophilus milk cannot be conveniently obtained, buttermilk may be substituted. For those patients who cannot take large quantities of sour milk, one of the more concentrated acidophilus preparations may be prescribed, care being taken that it is fresh and viable, namely, contains large numbers of live bacilli.

Abnormal intestinal microorganisms, as for example the streptococcus hemolyticus, are usually swallowed from some focus in the nose or throat, such as infected sinuses or tonsils. The source of the intestinal infection should be eradicated as completely as possible. If the abnormal organism is present in the stools in considerable numbers, an autogenous vaccine should be prepared, and the patient treated with it.

*Focal Infection.* Foci of infection, any place in the body, should be removed as completely as possible. All abscessed teeth should be extracted. If no other cause can be found to account for the chronic urticaria or angioneurotic edema, all devitalized teeth should also be extracted, even

though the X-ray shows no evidence of periapical bone destruction, as practically all pulpless teeth are infected.

Proper autogenous vaccine therapy is a valuable supplement to surgical or other treatment, in eradicating chronic infection. The preparation of autogenous vaccines, the selection of the proper organisms by means of intradermal vaccine tests, and the regulation of vaccine dosage, etc., have been dealt with in a preceding paper.<sup>11</sup>

#### EMERGENCY TREATMENT

Isolated attacks of acute urticaria are usually due to some dietary indiscretion, and are best treated by the prompt administration of a purgative. In urticaria or angioneurotic edema, when the symptoms are at all severe, the emergency treatment par excellence is epinephrine hypodermically. From 8 to 16 minims ( $\frac{1}{2}$  to 1 cc) of a 1 to 1000 solution of epinephrine should be injected, and repeated if necessary. Edema of the glottis may cause death. Therefore, in angioneurotic edema, when the edematous swelling seems to be affecting the throat or larynx, epinephrine should be administered without delay, and in sufficient dosage.

In chronic urticaria, epinephrine has certain disadvantages, in that it must be administered hypodermically to be effective, and the relief is of short duration.

Epinephrine solutions when fresh are colorless and clear like water. These solutions are relatively unstable, becoming readily oxidized upon exposure to the air, and are also affected unfavorably by exposure to light. Epinephrine solutions that have become darkened have lost considerable of their potency.



## SYMPTOMATIC TREATMENT

The itching in urticaria, which is frequently intense, may be relieved somewhat by one or more of the following antipruritic remedies: cold baths, either plain or with soda, sponging the skin with alcohol, or a saturated solution of menthol in alcohol, calamine lotion containing one per cent phenol, ointments containing menthol or phenol. Ice compresses may be applied to the localized swellings of angioneurotic edema.

*Bromides* Mixed bromides, 15 grains at a dose, should be prescribed, to be taken at bedtime when there is loss of sleep from itching, and two or three times a day when there is considerable nervousness.

*Ephedrine* Ephedrine, the alkaloid of ma huang, which has been used in Chinese medicine for over 5000 years, is the most valuable oral drug that we possess, for the symptomatic relief of urticaria and other allergic conditions. Ephedrine hydrochloride is preferable to ephedrine sulphate, as it contains about 5 per cent more of the alkaloid. Some of the first ephedrine sulphate that was put on the market, contained a considerable amount of pseudo-ephedrine and was consequently relatively inert.

Although ephedrine is not as potent therapeutically as epinephrine, and is somewhat slower in its action, it nevertheless possesses certain distinct advantages over epinephrine, namely, it is effective when administered orally, its action is of much longer duration, and the solutions are quite stable upon exposure to air and light, and will even withstand boiling.

Ephedrine hydrochloride for oral administration may be prescribed in capsules, tablets, or in a 3 per cent aqueous solution. The adult dose is from  $\frac{3}{8}$  to  $\frac{3}{4}$  grain (12 to 24 minims of the 3 per cent solution), the average dose being  $\frac{1}{2}$  grain (16 minims of the 3 per cent solution). The dose for children is from  $\frac{1}{4}$  to  $\frac{1}{2}$  grain (8 to 16 minims of the 3 per cent solution), with an average dose of  $\frac{3}{8}$  grain (12 minims of the 3 per cent solution).

## NON-SPECIFIC THERAPY

In urticaria, as in other allergic conditions, when the exact cause cannot be found and removed, some form of non-specific therapy should be resorted to. After having tried injections of sterilized whole milk, autogenous defibrinated blood, distilled water, horse serum, etc., I unhesitatingly recommend concentrated peptone solution, as it has given me by far the best results. I have found the commercial peptone solutions entirely unsatisfactory, probably because they are too weak. A sterile 33  $\frac{1}{3}$  per cent peptone solution should be prepared, after the method of Schiff,<sup>12</sup> containing equal parts of peptone siccum, glycerine, and water. Prior to treatment, the patient should be tested cutaneously with the peptone solution, as, if sensitization should exist, it would be extremely dangerous to inject the concentrated solution. The 33  $\frac{1}{3}$  per cent solution is given undiluted, the initial dose being one minim injected intradermally, the second dose two minims intradermally, the third dose three minims either intradermally or subcutaneously. For subsequent treatments the dose is usually increased by

one minim each time, depending upon the reaction in the individual case, until a maximum dose of sixteen minims (10 cc) is reached, then continued at this maximum dose. All doses larger than three minims, should be given subcutaneously. If it is preferred, the one and two minim intradermal doses may be omitted, and the treatments started with three minims subcutaneously. The peptone injections are given once or twice a week, usually the latter.

Desiccated peptone (peptone siccum) taken orally one-half to one hour before each meal, tends to temporarily desensitize against the various food proteins. It should be prescribed in capsules containing  $7\frac{1}{2}$  grains, one capsule to be taken one-half to one hour before each meal. Children are given 5 grain capsules, to be taken in the same way. Peptone is hygroscopic, namely takes up moisture from the air, and when it does, the powder contracts into a hard mass. In putting up peptone capsules, therefore, the capsules should be dusted inside and out with starch, and they should be dispensed in a tightly capped container.

### CASE REPORTS

Before closing, I will report briefly a few cases to illustrate some of the phases of treatment referred to.

A young woman was sent to me in May, 1925 with severe angioneurotic edema, which had started eight months before, following the extraction of an abscessed tooth. At various intervals since then, four other abscessed teeth had also been extracted. Her trouble started with swelling of the fingers, and then affected the toes and heels. The joints got red and swollen, and were very painful. The swelling would stay a day or

two in one joint and then jump to another. Her elbows and larger joints were not involved until later, and they were not as badly swollen. Two or three weeks after the trouble started, her lips became swollen, and the swelling gradually spread to other parts of her face. At times her eyelids were swollen shut. The swellings stung, and were very sensitive. Her body finally became practically covered with hives of various sizes, which lasted about 10 days. Although she still had them on her body, the swellings had recently involved principally her eyes and mouth. Her arms, legs, and body itched a great deal. At one time she had a very large swelling in her throat, which was relieved by an injection of epinephrine. I also found it necessary to administer epinephrine on three different occasions for the relief of marked swelling about her mouth. She had not been entirely free of urticaria or angioneurotic edema at any time during the preceding eight months. She thought that exertion, especially to the point of fatigue, aggravated her trouble. She also stated that eating chocolate made her break out in pimples. Her skin tests were all negative with the exception of a delayed positive reaction to chocolate and a positive reaction to orris root. She was advised to eliminate chocolate from her diet, and to avoid the use of face or body powders, etc., containing orris root. Her hemoglobin was only 76 per cent (Dare), for which she was given injections of iron. Cultures from the roots and sockets of the last two teeth extracted showed streptococcus hemolyticus and streptococcus viridans. When tested intradermally with autogenous vaccines of these organisms, she gave enormous reactions. The reaction to streptococcus hemolyticus was 4 inches in diameter, and viridans was 2 inches across. She was treated with these vaccines in gradually increasing doses, and the angioneurotic edema and urticaria disappeared. Her treatments were discontinued over three years ago, and she has had no recurrence of the angioneurotic edema, although she has an occasional small hive.

A woman, 27 years of age, consulted me in November, 1925 with angioneurotic ede-

ma, which she had been troubled with practically all of her life. Formerly, these attacks had occurred only in the spring, but in the preceding 6 or 7 years, they had occurred at all seasons. Each attack would usually last for 3 or 4 weeks. She would break out in great red blotches larger than the palm of her hand. The attacks often affected her eyelids, causing them to swell shut. There was no particular food that seemed to disagree with her, and she did not know of anything that would bring on an attack. She had tried various diets, etc., for the condition, but nothing seemed to help. Even injections of epinephrine failed to give complete temporary relief. She was gaining in weight, and had a subnormal temperature and a slow pulse. Her skin tests were all negative, with the exception of a few slight or doubtful reactions to substances which did not seem to have any bearing on her trouble. Her blood calcium was unusually low, namely 7.7 mgm per 100 cc, and her basal metabolic rate was minus 19. She was, therefore, given calcium, parathyroid, and thyroid orally, and ultraviolet light treatments. As a result she has had no further attacks.

A woman 43 years old was referred to me with angioneurotic edema, affecting principally her lips. The trouble had started about 6 years before, with attacks of swelling about the eyes, and an urticarial rash on the neck and various parts of the body. She had had a great many of these attacks at varying intervals, but in the preceding year, they had occurred much more frequently, and her lips had become affected. The attacks came on quite suddenly. The first symptoms noted were itching and burning of her lips. Then the lips would swell for several hours, until they were two or three times their natural size. They then looked as if they were filled with water, similar to a large blister. This swelling was accompanied with a feeling of tightness, and at times intense pain. After a certain amount of swelling, the lips would break open and discharge a sticky fluid which would dry and form crusts. When the lips would break, the tightness would be relieved, but they were very sore afterwards.

Each attack would last about a week, and they had a terrible effect on her nervous system. She thought that the trouble was due to eating sea food. She had been in the hands of a number of competent physicians, without results. Cutaneous and intracutaneous tests for protein sensitization were all completely negative. She had one devitalized tooth (upper left first molar) but there was no radiographic evidence of pathology. Her blood calcium was 9.2 mgm per 100 cc. The devitalized tooth was extracted, and cultures from the roots and socket showed staphylococcus pyogenes aureus in pure culture. Calcium and parathyroid were prescribed, and she was given ultraviolet light treatments, and injections of an autogenous vaccine prepared from the tooth cultures. She was discharged well, over a year ago, and has had no sign of trouble since.

A woman 41 years of age, was referred to me in August, 1927, with angioneurotic edema of six months duration. Although practically all parts of her body had been affected, the tissues around her eyes bore the brunt of the attacks. For temporary relief, she was given hypodermics of epinephrine, followed by ephedrine orally. Skin tests were all negative. Her red cell count was 4,070,000 per cubic millimeter, and her hemoglobin was 76 per cent (Dare). Her blood calcium was 9.7 (low normal). Calcium lactate, parathyroid, and solution of potassium arsenite were prescribed, and she was given injections of green citrate of iron. She was discharged entirely well, and when last heard from, there had been no recurrence of the angioneurotic edema.

A girl of 6 years was brought to me in January, 1928. She had been bothered with hives off and on since she was 14 months old. Her parents stated that her first attack of urticaria followed eating egg, and that she had not been able to eat eggs since, as they would break her out in hives in about ten minutes. The hives were usually worse around her mouth. Skin tests with the proteins of egg were completely negative. She gave instead a marked positive reaction to cottonseed protein. Eggs were returned to her diet, and all cottonseed oil products

(substitutes for olive oil and lard) were eliminated. Since then she has been entirely free of urticaria.

A woman 52 years old was referred to me with urticaria which she had been troubled with off and on since childhood. She stated that she was constipated and had a great deal of gas. She had chronic nasopharyngitis, and the discharge from her nose was yellowish in color. Her skin and hair were abnormally dry, and she had a subnormal temperature and a slow pulse. Her urine was of high specific gravity, very strongly acid, and contained a large amount of indican. Her basal metabolic rate was minus 11, and her blood calcium was 9.4 mgm. Cultures from her nasal secretion and throat showed staphylococcus aureus and streptococcus hemolyticus, and cultures from her stool also showed streptococcus hemolyticus. She gave marked positive reactions to intradermal tests with autogenous vaccines of these two organisms. She was

advised to drink more water, and eat more of the alkaline foods, and less of the acid-forming ones. Calcium, parathyroid, and thyroid were prescribed. Acidophilus milk was also advised. She was given injections of the aureus and hemolyticus vaccines at weekly intervals, in gradually increasing doses. As a result she has had no more urticaria.

### SUMMARY

Urticaria and angioneurotic edema are of frequent occurrence, and present to the physician one of his most difficult therapeutic problems.

In this paper, based upon a careful study of 160 patients with urticaria or angioneurotic edema, a comprehensive method of treatment is described, and illustrated with excerpts from case histories.

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# Obesity

## Procedure, Classification, Treatment, And Results, In 151 Cases Studied During The Past Six Years, With Special Reference to An Endocrinopathic Origin.\*

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**M**UCH has been written on the subject of Obesity, and the literature on the study of the condition is certainly voluminous. However, there still remains a vast amount to be uncovered, and explained. Recently there have appeared several expressions of doubt as to an endocrinogenic factor in obesity,<sup>1,2</sup> and placing its incidence below one per cent. No "normal healthy adult" measures his food intake in grams of carbohydrate, fat and protein, and then, to keep his weight stationary, proceeds to work and exercise, play and rest in a measured caloric-equivalent amount. Still, some will gain weight, while others on the comparatively same, or identical schedule will lose weight. This truth, so well known to all, layman and scientist, is proof enough that even in many so-called simple exogenous obese, there must be other underlying disturbances—metabolic and endocrine.<sup>3,4</sup> Therefore, an analysis of the study and treatment of 151 cases during the past six years, helps to cast some light on the effects of treatment, and on the consideration of etiology.

### DEFINITION

No case was considered obesity, unless the weight, for the sex, age, height, and configuration, was at least 20% greater than the standards given as normal.

### PROCEDURE

Having thus admitted a patient as "obese," a routine procedure was instituted.

- 1 History, with special reference to family history of Endocrinopathies and Obesity, personal history pointing to endocrine disease and weight curve, menstrual, marital, and sex history, appetite and food intake, exercise, etc.
- 2 Physical Examination, with special reference to endocrine signs, fat distribution, hair, teeth, skin, sex organs, measurements, etc.
- 3 Laboratory examinations, especially, X-Ray of sella turcica, sugar tolerance, X-Ray of thymus, basal metabolism, and blood chemistry.
- 4 Each patient brought us his or her food consumption over a period of 5 days (without change from previous routine), and daily work and exercise chart.

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## CLASSIFICATION

With this data before us, each case was placed into its proper category in the following classification

- 1 *Exogenous*—where no abnormal findings (physical or laboratory) were revealed, and where the food intake was sufficiently high, in proportion to the work and exercise, to warrant considering a positive caloric balance
- 2 *Endocrinopathic*
  - (a) Pituitary disease—as evidenced by girdle obesity, small sella turcica, delayed menses or amenorrhea, deficient sex organs, increased sugar tolerance, etc
  - (b) Thyroid disease—present or absent struma, low basal metabolism, slow pulse, myxedematous infiltration, etc
  - (c) Thymic origin—type, low blood pressure, deficient sex apparatus, positive Thymic X-Ray, etc
  - (d) Pre-diabetic type—as shown by marked sugar tolerance decrease
  - (e) Gonadal type—trochanteric obesity, castration, menopause, etc
  - (f) Mixed types—pluriglandular disease
- 3 *Idiopathic or Constitutional*<sup>s</sup>—a group of unexplained obese,—not exogenous, and not affected by any or all types of treatment

The 151 cases were divided as follows

- 81—Exogenous
- 46—Endocrinopathic
- 20—Idiopathic or constitutional etc
- 3—Lipomatoses, Lipodystrophy, etc
- 1—Dercum's Disease

The 46 Endocrinopathic cases were redistributed as follows

Pituitary	28
Thyroid	10
Thymic	2
Pre-Diabetic	2
Gonadal	2
Mixed	2

## TREATMENT AND RESULTS

The exogenous cases were placed on a diet as follows

"Take only half of the quantity of each food that you are accustomed to take! Use no desserts that are prepared with flour or sugar! Take at least one fresh fruit and vegetable three times a day! The following articles of diet are recommended because of their low fat and carbohydrate (sugar and starch) content—these two elements of food being the principal fat producing and fat saving agents of food<sup>o</sup>

"*Animal Foods*"—To be baked, broiled or boiled except where indicated otherwise Lean chuck, loin and round steak, lean ribs of beef, all ground or cooked whole, lean leg of shoulder, loin and roast or veal Lean chicken and other fowl, except goose, turkey, duck or squab All fresh fish except butterfish, salt water eel, salmon and shad May take clams, crabs, lobsters No pork in any form to be taken

"*Dairy Products*" — Buttermilk, skimmed milk, cottage cheese (the only variety of cheese allowed) eggs in any form allowed, except fried No butter!

"*Pickles, Condiments*" — Tomato catsup, horseradish, vinegar, sour cucumbers, pickles, cabbage and cole

slaw Pepper not allowed Salt used sparingly

*"Fresh Fruit"*—All fresh fruits may be used in moderation Any fruit may be cooked in any form if sugar is not used in their preparation

*"Nuts"*—All nuts are fat except chestnuts and are not to be eaten Not over six (6) chestnuts should be eaten in one day

*"Fresh Vegetables"*—The following may be used—Asparagus, celery, brussels sprouts, lettuce, cucumbers, endive, spinach, rhubarb, sauerkraut, cauliflower, egg plant, green peppers, kohlrabi, leeks, radishes, string beans, cabbage, okra, turnips, and onions

*"Bread"*—No bread may be used

*"Cereals"*—Not over a tablespoonful of any breakfast food after it is cooked, with equal amount of Kellogg's bran mixed with it If milk and sweetening are required, use skimmed milk and sugar substitutes

*"Drinks"*—No beers, wine, nor heavy liquors Black coffee or tea once a day Use skimmed milk, butter milk, and no sweet soda fountain drinks may be taken

The change in weight at the end of six months varied from a gain of 2 lbs to a loss of 70 lbs, average 44 lbs lost In some cases (17) thyroid was added in doses varying from  $\frac{1}{2}$  grain to 5 grains (daily)—and a definite increase in loss of weight was observed The pulse rate was not permitted to get above 90, (taken after reclining 20 minutes)—and any symptom or sign of excessive thyroid medication called for a rest of 5 to 10 days Not one example of ill effects was observed We firmly believe that though a certain degree of

danger exists in the use of thyroid substance, it is minimal, or nil, when the patient is well controlled and observed<sup>7</sup>

The endocrinopathic group received the diet and exercise treatment, plus organo-therapy, as indicated On diet and exercise alone this group lost 21 lbs average, per person, during a trial period of 6 weeks Our largest group, the pituitary group, received pituitary substance by mouth in doses from 10 to 30 grains daily, with posterior pituitary solution by injection, varying from  $\frac{1}{2}$  cc twice weekly to 1 cc daily The addition of thyroid gland by mouth aided the reduction materially, although some definite loss occurred usually without it The loss of weight in 6 months in this group varied from 3 lbs to 92 lbs average per person for 6 weeks, 13 lbs

The idiopathic or constitutional group failed to respond to any type of treatment, or diet restriction, including low caloric diet, salt free diet, water restriction, etc This group impressed us as a type of pluriglandular disease, with some missing incretion, but on the whole they cannot take thyroid substance without symptoms

#### B M R OBSERVATIONS

An observation of note was made in 22 cases, where the B M R was found increased, between 12% and 34%, unexplained by any previous drug therapy or gland therapy We disregarded this in our treatment This observation has been made by others<sup>8,9</sup> and the explanation is as yet purely theoretical

## SUMMARY

The classification of 151 cases studied during the past six years is given

The method of classifying and treatment is outlined

The results are briefly stated

Increased B M R were observed in about 15% of all the cases studied

## CONCLUSIONS

Obesity, regardless of type, can in a large measure be reduced,—excepting a group, which for want of a better term, is as yet labelled Idiopathic or Constitutional. Diet alone—reduction in caloric intake to below caloric expenditure—cannot affect all obese to produce weight reduction. Endogenous obesity is not a myth,

nor a misconception, while exogenous obesity has often an endogenic or endocrinous etiological factor. Finally, we think, that if we group together all the cases of obesity, we will have at one extreme, the purely exogenous obesity, and at the other extreme, the purely endogenous obesity, of various types, but between these extremities the greatest group of mixed cases, all with a metabolic defect,—and here and there a so-called idiopathic or constitutional case. In treatment, all these things must be borne in mind. The problem is too complex, to be treated by so simple a formula as mere diet reduction, but instead we must add organo-therapy and other measures as indicated.

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# A Case of Pregnancy Complicated by Cardiac Decompensation and Anemia Gravidarum

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**D**URING the past few years the attention of both obstetricians and internists has been actively engaged by the problem of cardiac disease in pregnant women. Some interest has developed also in that curious type of essential anemia which is occasionally associated with the pregnant state. It seems worth while, therefore, to record a case which presented both of these complications, each in a severe form.

## REPORT OF CASE

Mrs. C. B., an Italian housewife of 36, entered the Waltham Hospital on February 1, 1928, early in the eighth month of her fourth pregnancy.

The only significant item in her past history was rheumatic fever, of which there had been two attacks, ten years and one year previously. The obstetrical history of the first three pregnancies was uneventful.

The present illness began two months before admission, with cough, dyspnea, and malaise. The patient was treated by another physician for bronchitis, but all her symptoms grew steadily worse. The cough became constant, with profuse expectoration, dyspnea and prostration increased, and she began to have gastric distress after eating, frequently vomiting undigested food.

Examination revealed first of all a marked pallor. The heart was enlarged to the left, to the right, and downward, and a soft blowing systolic murmur was heard over the whole precordium. The lungs showed no dulness, but scattered râles were audible on

both sides. The uterus was enlarged to the size of a seven months' pregnancy, the fetus lying in the right sacroanterior position. On vaginal examination the introitus was found to be roomy, the cervix was long and hard. Pelvimetry gave normal bony measurements.

On admission the red blood count was 2,500,000 and the hemoglobin 55 per cent, the stained smear showed nothing definitely abnormal except achromia. The urine was essentially negative. Four examinations of sputum failed to reveal tubercle bacilli. X-ray of the lungs showed increased lung-markings on the right, and small areas of increased density on both sides.

After careful consideration, we decided to institute treatment for the cardiac condition and the anemia, and, in event of definite improvement, to allow the pregnancy to continue either to term, or at least until such time as the baby's chances would be better.

The cardiac decompensation was treated by rest, sedatives, and different preparations of digitalis. Glucose also was given both by rectum and in small amounts intravenously. For the anemia the patient received, in addition to suitable diet, injections of liver extract. Transfusion was considered and rejected, mainly because of the extra load which a sudden increase in the blood-volume would throw upon an already laboring heart.

In spite of these measures the hoped-for improvement did not manifest itself. The cardiac condition remained the same, dyspnea and cough were exhausting the patient's strength, and the congested stomach

was retaining only a small part of the food taken. The anemia, on the other hand, grew more and more severe, on February 19 the red count was 2,040,000 and the hemoglobin was reduced to 35 per cent. Thus it became obvious that the mother's life would surely be sacrificed if the pregnancy were allowed to continue further.

On February 22 the patient was delivered by caesarean section, under scopolamine-morphine and local novocaine anaesthesia. Sterilization was done by the Madlener method. The operation was remarkable chiefly for the exceedingly small amount of blood lost. The child, a healthy male weighing six pounds, showed no evidence of prematurity, and did well from the start.

For the first week the convalescence was stormy. All the previous symptoms persisted, requiring a careful balancing of sedative and stimulant treatment. Extreme restlessness and some air-hunger developed. On February 25 a transfusion of 600 c.c. of blood was done by Dr. H. Quimby Gallupe. For several days thereafter frequent inhalations of oxygen were given.

On the second week the gastric congestion subsided, and the patient became able to take and retain a normal diet. The third week was marked by a diminution in the cough. From that time on the cardiac condition improved steadily, until compensation was fully established.

The improvement in the blood was striking. On March 4 the red blood count was 3,600,000 and the hemoglobin 50 per cent. On April 9 the red count had risen to 4,500,000 and the hemoglobin to 65 per cent.

The incision failed to heal by primary union, as not uncommonly happens with profoundly anemic tissues. Nevertheless a sound scar was ultimately obtained.

Now, a year after delivery, the patient considers herself to be in good health. She is able to lead a normal life and to perform her domestic duties without any obvious incapacity.

#### DISCUSSION OF CASE

This patient presented the most serious cardiac complication of preg-

nancy—broken compensation which fails to improve under treatment. If she had been seen earlier, abortion would have been imperative. If she had reached full term, the question would have arisen whether she might be delivered with less risk by caesarean section or by a forceps-operation eliminating the second stage of labor. As the situation actually was, we felt that immediate delivery was indicated, and that caesarean section was safer than the double procedure of induction of labor and delivery from below. The opportunity to do sterilization was undoubtedly advantageous, but did not influence us to choose abdominal delivery. Regarding anesthesia, in our opinion ether was absolutely contraindicated by the pulmonary condition, though it might have been tolerated by the heart.

The anemia in this case was of the type that has been called puerperal anemia, or chronic hemolytic anemia due to pregnancy. The second name is cumbersome, the first is not strictly accurate, since the disease may develop in the late months of pregnancy (as in our present case), as well as during the puerperal state. Hence we prefer the more general term anemia gravidarum.

This condition must not be confused with pernicious anemia. Gallupe and O'Hara<sup>1</sup> say "Pernicious anemia is the name of a definite disease syndrome, and should not be used as a descriptive name for any profoundly anemic condition. Puer-

<sup>1</sup>GALLUPE, H. QUIMBY, and O'HARA, DWIGHT. Puerperal Anaemia. Boston Medical and Surgical Journal, Vol. 190, No. 5, pp. 161-164, Jan. 31, 1924.

peral anemia is an entity in itself, and should not be called pernicious anemia associated with pregnancy." It should be distinguished also from the anemia consequent upon hemorrhage and from that due to sepsis.

True anemia gravidarum is a grave condition, which in spite of all medical treatment becomes progressively more severe and terminates fatally in

a majority of cases. Transfusion is a life-saving measure, it produces an immediate improvement and usually tides the patient over until complete recovery is established.

This case emphasizes again the need for the closest cooperation between the obstetrician and internist in handling the serious medical complications of pregnancy.

# Undulant Fever

## Report of Five Cases

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JUDGING from the medical literature of the past two years it seems that I am one of the few remaining physicians in the United States who has not reported one or more cases of undulant fever. I therefore hasten to add my quota.

No attempt is made to review the literature or to discuss anything of the distribution, etiology or bacteriology of this disease as these features are necessarily fresh in the minds of every one.

Two of these cases perhaps have points of interest in that one of them was not affected in any way by the intravenous use of mercurochrome (some writers have reported immediate cures following such treatment) and another seemed to show no encouraging results from the use of a one (1) per cent solution of tartar emetic intravenously.

The five cases were seen at the Station Hospital, Fort Sam Houston, Texas, during the years 1924, 1925, and 1926. Unfortunately no absorption agglutination tests to differentiate *B melitensis* and *B abortus* were made in these cases, although the procedure was carried out later in other cases, notes on which are not available at this time. Also all the blood

cultures were negative for *B melitensis*. Thus the diagnosis in each case is based almost entirely on the elimination of other diseases and the positive agglutination tests for *B melitensis*, although in Cases I and II the history and the clinical course are quite typical.

The case histories are reported as briefly as possible.

### *Case I*

B N C, white, male. Age thirty-two years. Admitted September 7, 1924. Family history Unimportant. Previous personal history Hookworm at fourteen or fifteen years of age. Malaria in 1916. Amebic dysentery, 1916. Gonorrhea in 1920. Had spent a great deal of time in Mexico for the previous three years, where he used, frequently, goats' milk and cheese made from goats' milk.

Two weeks before admission to hospital he was sick at Laredo, Texas, with "Intestinal fever." Had headache and pain in various regions of body. On admission to hospital felt weak but had no particular complaints.

Physical examination Nothing remarkable.

Briefly, the patient went through a four and one-half months' course of undulant fever, apparently unaffected by any treatment. The graphic temperature chart shows the duration of the exacerbations and remissions to be as follows. Exacerbation seventeen (17) days (Temperature up to 104.4° F, lysis), remission five days, ex-

acerbation twenty-four (24) days (temperature up to 105.2° F, lysis), remission three days, exacerbation thirteen days (temperature up to 101.8° F, lysis), remission three days, exacerbation seven days (temperature to 99.6° F), remission six days, exacerbations for one or two days at irregular periods, temperature going from 99 plus to 100, for forty-three days, then an exacerbation for eight days (temperature up to 102.6° F, lysis)

There were occasional slight P M elevations of temperature for three months after the last fever curve and the symptoms of weakness, joint pain, and constipation were present more or less over most of this period. No enlargement of the spleen was noted at any time.

The urine was negative except that, during the temperature rises, albumin and hyaline casts were present frequently. Urine cultures negative for typhoid. Stools (four) were negative for parasites and one stool culture negative for the typhoid group. Blood (two) negative for malaria. Some of the blood pictures were as follows: September 28, 1924—R B C 4,220,000, W B C 10,450, Hem 80%, S M 30%, Polys 65%, Eosin 4%. October 13, 1924—R B C 3,900,000, W B C 6,300, Hem 80%, Polys 60%, Eosin 2%. October 28, 1924—R B C 4,180,000, W B C 8,150, Hem 80%, Polys 60%, Eosin 2%. November 28, 1924—W B C 6,000, Polys 45%, Eosin 5%. Blood culture negative for typhoid group. Blood culture (two) negative for *B. Melitensis*.

Melitensis agglutinations: October 15, 1924—Positive plus (1-640 dilution). October 16, 1924—Positive double plus. January 5, 1925—Positive plus (1-320 dilution). June 18, 1925—Positive plus.

Blood Wassermanns (three) were double plus early in the disease but later all Wassermanns and provocative Wassermanns were negative. Blood chemistry normal.

The treatment was entirely symptomatic except that

1 Quinine was given by mouth for a period with no results.

2 Neoarsphenamine 0.3 gms was given

on one occasion with no results. (On the second day of the second rise of fever.)

3 Mercurochrome (15 cc of a 1% solution) was given intravenously once during the height of an exacerbation with no result except a quite severe general reaction. (On the tenth day of the second rise of fever.)

### Case II

E. H., white, female. Age thirty-two years. Admitted January 2, 1925. Family history: Unimportant. (This patient was the wife of a medical officer of the army who was a laboratory specialist and who had been doing considerable work with Malta fever for the previous few months. History revealed no other opportunity for infection with *B. melitensis*.) Previous personal history: Malaria at eleven years. Typhoid at sixteen years. Otherwise unimportant. Present illness: On December 6, 1924, had feeling of marked depression, that night a slight chill. For three days following had severe headache. From then until December 25th was up part of time and in bed part of time with headache, pain in back, chilliness, etc. Appetite very poor. Constipated. On December 25, 26, 27, and 28, had severe chill about 4:00 P M. Had severe headache and some fever each time. Temperature persisted, going up to 102° F plus. Cough developed and on afternoon of December 31st had slightly blood streaked sputum. None afterward. Had lost twelve pounds in past three months.

At time of admission complained of headache, slight, dry cough, marked weakness, heavy drenching sweats occasionally in afternoons, poor appetite, marked constipation.

Physical examination showed nothing of note other than a prolapsed uterus. Well nourished. Spleen not enlarged. Urine and stools negative.

Blood Counts: January 3, 1925—R B C 4,350,000, W B C 7,200, Hem 80%, Polys 67%. January 5, 1925—R B C 4,100,000, W B C 7,150, Polys 70%.

January 3, 1925—Blood negative for malaria. January 7, 1925—Blood negative for malaria. Blood Wassermann negative.

Blood Cultures January 2, 1925—Four specimens at two hour intervals were negative (no growth)

Blood Agglutinations January 3, 1925—B melitensis positive, double plus January 6, 1925—B melitensis positive, 1-1280 dilution Typhoid, Para A and Para B negative January 11, 1925—B melitensis, positive 1-2500 dilution January 4, 1925—Urine culture negative

Fever continued for twenty-four days, with morning remission and afternoon rise up to 102.4° F There was then a remission lasting for fourteen days and she was allowed to go home

Symptoms during stay in hospital were the temperature, chilly sensations followed by sweating, marked physical and mental depression, fleeting joint pains in various joints, and constipation The spleen was never palpated

The symptoms of physical and mental depression and occasional slight elevations of temperature persisted for some months after leaving the hospital but there was no actual prolonged curve as seen in Case I

Treatment was symptomatic

### Case III

W M, white, male Age twelve years Admitted July 12, 1926 Family history Mother died of carcinoma of cervix uteri One brother has tuberculosis of right hip Otherwise unimportant Previous personal history Scarlet fever in early childhood Tonsillectomy in 1921 Triple typhoid inoculation (three injections) in 1921 About three and one-half weeks before admission patient had an attack of sore throat which lasted two or three days during which he had fever ranging from 100 to 104° F After the attack of sore throat disappeared the fever persisted, within the variations above noted, otherwise he felt fairly well No headache Occasional pain in the abdomen Bowels had been moving two or three times daily in past week

Only complaints on admission were of occasional pain in abdomen, two or three fairly loose bowel movements daily for past week, temperature of from 100 to 104° F for past three weeks

Physical examination was negative except for slight gaseous distention of the abdomen X-ray of chest negative The urine negative Stool culture negative for typhoid group Blood count R B C 4,090,000, W B C 6,150, Hem 80%, Polys 32% July 12, 1926—Agglutination for typhoid fever 1-160 Paratyphoid A and B negative Malta fever positive, 1-1200 July 13, 1926—Blood culture negative for typhoid group July 15, 1926—Agglutination positive for B melitensis 1-1000 July 22, 1926—Agglutination positive for B melitensis, 1-1000

The temperature persisted from 102.6° F, gradually declining by lysis to normal over a period of eight days, then two days remission and a slight rise of temperature again to 100° F, thus exacerbation lasting three days The original temperature curve thus lasted for about thirty-two days The only symptom noted in hospital was slight headache There were no gastrointestinal symptoms The spleen was not palpated at any time Convalescence was slow but uneventful Treatment symptomatic

### Case IV

L B F, white, male, age seventeen years Date of admission July 22, 1926 Family history Unimportant Previous personal history Unimportant History of present disease Had been feeling badly for several days before admission to hospital, with some malaise Was in infirmary at the military academy, where he was attending school, for several days before admission to hospital At time of admission seemed dull mentally and complained of dizziness when in the erect position Physical examination showed an occasional cardiac extra systole, a few sibilant râles in the lungs posteriorly, otherwise negative. Spleen not enlarged

X-ray of chest negative Urine showed a trace of albumin, otherwise negative Stools negative for parasites

Blood Counts July 23, 1926—W B C 4,750, Hem 70%, Polys 53% July 24 1926—W B C 8,950, Hem 80%, Polys 70% July 27, 1926—W B C 6,200, Polys 47% July 28, 1926—W B C 4,950, Polys 64% Blood negative for malaria on July

23, 1926 and July 24, 1926 On July 27, 1926 the blood agglutination for typhoid fever, 1-80 Para-typhoid A 1-80, Para-typhoid B 1-160 B melitensis 1-1200 Blood culture negative July 28, 1926—Stool culture negative for typhoid group July 30, 1926—Blood agglutination, typhoid 1-80 Para-typhoid A 1-80 Para-typhoid B 1-160 B melitensis 1-1200 July 31, 1926—Blood culture negative for typhoid group and for B melitensis August 17, 1926—Blood agglutination positive for B melitensis 1-650

The temperature on admission to the hospital was 100.1° F The day following it was 104° F and thereafter ranged from 105.2° F, gradually declining by lysis to normal over a period of twenty-seven days, it was then normal for twenty-four hours when it was again elevated to a maximum of 103.8° F, declining by lysis over a period of eight days Following this there was a normal intermission for four days, followed by an elevation to 100° F, for two days, after which it continued normal The pulse rate was proportionate to the temperature Respirations within normal limits

The only symptom other than the temperature was constipation Treatment symptomatic throughout Discharged from hospital on August 26, 1926, feeling perfectly well and had no symptoms thereafter

#### Case V

C H W, white, male Age twenty-one Date of admission October 11, 1926 Family history Unimportant Previous personal history Unimportant History of present disease For one week before admission to hospital he had noticed that he felt "weak and feverish" in the afternoons and had dull pain in the back and abdomen The day previous to admission the weakness was marked, there was vertigo, and the pain in the back and abdomen was increased Symptoms increased during the day, leading to his being sent to the hospital the following morning

On admission he complained of slight cough, dull aching pain in abdomen and back, weakness and dizziness when in erect position

Physical examination Showed a slight generalized adenopathy and some tenderness to pressure over lower abdomen X-ray of lungs negative Of four specimens of urine examined one showed albumin Stools negative

Blood Counts October 15, 1926—R B C 4,670,000, W B C 6,350; Hem 80%, Polys 66%. October 16, 1926—W B C 5,200, Polys 62% October 18, 1926—W B C 5,400, Polys 64% October 28, 1926—W B C 4,800, Polys 58% November 6, 1926—W B C 6,700, Polys 58% December 16, 1926—W B C 7,250, Polys 65%

Blood negative for malaria Blood Wassermann negative Blood culture negative Blood agglutination negative for typhoid group, positive for B melitensis, 1-1200

November 17, 1926—Blood agglutination positive for B melitensis 1-600 December 15, 1926—Blood agglutination positive for B melitensis, 1-320

Four days after admission it was noted that the spleen was enlarged and tender Patient was running a high temperature No other symptoms except the enlarged and tender spleen and marked constipation He was given tartar emetic, 1% solution, intravenously as follows October 18, 1926—Three (3) cc October 25, 1926—Four (4) cc November 1, 1926—Five (5) cc November 8, 1926—Six (6) cc November 15, 1926—Seven (7) cc

Treatment otherwise was entirely symptomatic The temperature persisted, having declined by lysis, until November 10, 1926, a period of thirty days Following this it remained normal and there were no further symptoms of any kind

Although the fact of the patient having previously had the triple typhoid vaccine is mentioned in but one case, it should be stated that each had had one or more courses of this vaccine at varying periods prior to the present illness, this undoubtedly accounts for the 1-160 agglutinations for typhoid in Case III and the 1-80 typhoid, 1-80 para A and 1-160 para B agglutinations in Case IV. It is

believed that the typhoid group was eliminated as the etiological factor in both cases, certainly they did not appear clinically to be typhoid

As further items of interest it may be noted that the spleen was enlarged in but one case, sweating was present in but one case, joint pains occurred in two cases, constipation was a definite factor in four cases. No joint pathology was noted, only the complaint of pain. In one case there was slight frequency of the bowels (2 to 3 daily stools) for a week before admission to hospital.

In all cases the white blood count was normal or showed some leucopenia

and the polymorphonuclear count tended to be low. The onset was insidious in four of the cases.

Cases I and II had a suggestive history for *B. melitensis* infection and it is of interest that both had a rather typical clinical course with a long drawn out convalescence. The three other cases had histories which were not suggestive (although all were milk users), a shorter total period of febrile reaction, seemed less ill and convalesced quickly.

Might we assume that Cases I and II were *B. melitensis* infections and Cases III, IV, and V, *B. abortus* infections?



## Editorials

### *LESIONS OF LATENT SYPHILIS*

The following consists of abstracts from a paper read by the editor in opening a discussion in the Section of Venereal Diseases at the Annual Meeting of the British Medical Association, Manchester, July, 1929, and is here reprinted at the request of a number of members of the College

#### *Leptomeninges*

Lesions of latent syphilis occur very frequently in the meninges, being present in the great majority of cases. They vary greatly in intensity, from small, localized opacities or thickenings to more patchy or even generalized thickenings of the arachnoid and pia. They are found most frequently over the parietal and frontal lobes, usually over the sulci, and not over the convolutions. In the active latent lesions these meningeal thickenings and opacities appear microscopically as localized areas of a mild productive process with slight infiltrations of monocytes, plasma cells, and lymphoid cells. There is a proliferation and increase of the reticulo-endothelial cells of the membranes, with eventually cells of fibroblastic type leading to fibrosis. Small perivascular collections of lymphocytes and plasma cells may occur throughout the meninges, the number and degree of these being in proportion to the severity of the process. In many cases

there is only a slight productive reaction, leading slowly to thickening and hyaline change in the membranes. The sharply localized character of these mild lesions is very striking. Often they are seen in the gross with difficulty, by oblique light or upon floating the membrane. In the old case of latent syphilis the process may be for the greater part healed or inactive, the membranes show hyaline thickening, while cellular areas may be found only after prolonged search. Every transition stage of severity may occur, from slight fibrosis of the meninges to the active and clinically recognizable form of syphilitic meningitis.

#### *Brain*

Localized perivascular infiltrations occur within the brain tissue of the latent syphilitic. They are precisely similar to those found in paresis and cerebral syphilis, the difference being only in number and degree. They occur usually throughout the frontal and parietal lobes, and near the ventricles. They are usually few in number, in some brains only one or two such infiltrations may be found on extensive examination microscopically. Here again all transition stages in degree and number of these lesions occur, up to active brain syphilis and paresis. In many cases of syphilitic psychoses these latent lesions are found in very moderate numbers associated with a moderate atrophy and gliosis of the

brain tissue, involving particularly the frontal lobes. It may be said that every latent syphilitic has localized lesions identical with those of paresis, the only difference being in the number and intensity of these lesions. The meningeal lesions and those of the brain tissue do not always show a corresponding degree of involvement, as a rule the meningeal lesions are more numerous and more marked than the cerebral.

#### *Spinal Cord*

Similar lesions are found in the meninges of the cord and in the cord itself, but less frequently than in the brain.

#### *Heart*

In my experience the heart of every male latent syphilitic has shown latent lesions, varying from small and few microscopic areas of increased stroma nuclei and plasma cell and lymphocyte infiltrations up to more diffuse areas of interstitial myocarditis. In the majority of latent syphilitic females these cardiac lesions do not occur, or are very small. Nevertheless, in some women more severe forms of syphilitic myocarditis do occur. The part of the heart usually involved in these latent lesions is the septum, and the anterior and posterior walls of the left ventricle near the apex, rather than the walls of the right ventricle, although in some cases the right ventricle has shown more marked involvement than the left. The lesions are usually intermuscular, rather than perivascular. In the mildest degree they consist of an increase in the number of stroma nuclei, the latter being arranged in single or double file, occasionally with large ag-

gregations of nuclei between the muscle. These aggregations represent perivascular infiltrations around the smallest coronary branches. The infiltrations present a variety of cell forms: plasma cells, lymphocytes, monocytes, and cells of fibroblastic type. Occasionally polynuclears are present. The chief characteristic of these infiltrations is their diffuse or patchy character. They are not sharply demarcated, but trail off irregularly into the neighboring heart muscle. The papillary muscles are often involved. Very characteristic is an increase of nuclei beneath the endocardium, the cells lying in two to five rows, closely crowded together. They appear to be derivatives chiefly of the subendothelial reticuloendothelial cells. The stroma often appears markedly edematous, as in congenital cardiac syphilis, and very frequently it gives a mucoid reaction with mucin-staining dyes. The more active the process, the more marked is the edema. Fibrosis of the myocardium is the eventual result of this interstitial proliferation and infiltration. Between the active infiltrations the heart muscle fibers are well preserved, often hypertrophic. As the active cellular infiltration diminishes and fibrosis results, the heart muscle becomes atrophic, and often shows fatty degenerative infiltration. In many cases the fibrosis of the stroma takes place without much change in the muscle fibers. Ultimately, however, atrophy of the muscle results, and there is a patchy fibrosis of the myocardium containing atrophic fibers. This latter distinguishes infarct scars from the syphilitic fibrosis, the former being more sharply circumscribed and

devoid of muscle fibers in their central portions, at least Spirochetes may be found, often after prolonged search, in the active infiltrations, and even in the scar tissue, when the latter is still fairly cellular. When the fibrosis becomes hyaline it is impossible to find them. Hence the advantage of the Warthin-Starry method of straining spirochetes in single sections, permitting control of the histologic lesions. With the exception of the aortic, the valves are rarely involved in latent syphilis. The aortic valves are affected chiefly through the vasa vasorum of the aorta, and a certain degree of sclerosis of the aortic valves is almost always present in the latent syphilitic in later years. Acute exacerbations of the latent lesions occur without known cause, and are characterized by a polymorphonuclear infiltration, in which spirochetes are present.

The heart of the latent syphilitic usually shows at necropsy dilatation of the left ventricle or of both ventricles. In the great majority of cases there is no valvular lesion, although the sequela of bacterial endocarditis may be coincident in some cases. In the younger individual latent syphilis of the heart probably predisposes to secondary bacterial endocarditis, as numerous cases showing this combination have been observed. In the older cases the majority show no secondary valvular involvement. The great majority of cases of latent syphilis come into the clinic of internal medicine as patients showing more or less vague myocardial insufficiency, with symptoms of dyspnea, palpitation, slight or marked cyanosis, and chronic passive congestion. They represent a definite cardio-

vascular complex. When questioned as to the occurrence of rheumatic symptoms they almost invariably give affirmative answers, and the common clinical diagnosis is therefore "rheumatic heart," even in the absence of all evidence of valvular lesion. A progressive course downhill of increasing cardiac dilatation and insufficiency follows, and the cause of death in the latent syphilitic is most frequently "cardiac or myocardial insufficiency." To what extent this cardiac failure is due to the myocardial lesion or to the associated aortic lesions is usually very difficult to determine. At necropsy the heart is dilated, the wall thin and atrophic, with a certain degree of subendocardial fatty degenerative infiltration. The endocardium is usually more or less thickened and opaque. Cross-section of the heart wall will show more or less marked irregular areas of fibrosis, particularly in the left ventricular wall towards the apex. A cardiac death is a very frequent form of death for the latent male syphilitic, and a large percentage of the deaths occurring in middle life from "myocardial degeneration" are due to this cause.

#### *Aorta*

Latent active lesions are found in the aorta of every male syphilitic and in the majority of female syphilitics, although usually they are much less marked in the women than in the men. The lesion is essentially a disease of the vasa vasorum, consisting in obliteration and thickening of the walls of the small nutrient arterioles of the aorta, with plasma cell and lymphocyte infiltrations along the course of these vessels. The term "mesaortitis" is a

misnomer, as syphilis of the aorta does not affect primarily the muscle coat of the vessel, but is primarily localized in the vasa vasorum. The infiltrations are always more marked in the adventitia around the larger vasa vasorum than in the media, decreasing in size towards the intima. As the result of the obliteration of the nutrient vessels there is a slow infarction of the intima and inner portion of the media, resulting in sclerosis and atrophy of the muscle and degeneration of the yellow elastic tissue. In the mildest cases small infiltrations are found only in the adventitia and around the para-aortic blood vessels. The gross pathological picture in the mild cases of aortic syphilis is that of an area of aortic sclerosis or atherosclerosis. In many cases it cannot be diagnosed as syphilitic in character from the gross appearances. Even in aortas that appear normal latent syphilitic lesions can be found in the adventitia around the vasa vasorum. The gross appearance of any aorta cannot be taken as a criterion for the absence of active syphilitic lesions in its wall, only the microscopic examination can decide as to the absence or presence of syphilis. It is in the severe forms of aortic syphilis that characteristic lesions of syphilis show grossly in the form of irregular fissures and depressions in the intima with the characteristic porcelain-blue appearance. In the great majority of cases, however, the changes produced in the aortic wall by syphilis are covered up by the associated secondary sclerosis of intima and inner portion of the media.

Syphilis of the aorta may exist in three forms with aneurysm, with

aortic insufficiency and in the form of perivascular lesions around the vasa vasorum in the absence of both aneurysm and aortic insufficiency. The third form is by far the most common, but is rarely recognized by the clinician. It may be either symptomless, or present the clinical syndrome of an aortalgia, or even that of angina pectoris. In the cases associated with aortic insufficiency the valvular lesion is the result of an extension of the syphilitic disease of the vasa vasorum of the aorta to those of the valves. In the cases with aneurysm the weakening of the aortic wall is usually due to a localized development of miliary gummas along the vasa vasorum in their course through the media. As in the case of the heart, acute exacerbations of latent aortic lesions occur without known cause. They are also characterized by a polymorphonuclear infiltration, and frequently by localized necrosis in the media. Spirochetes are easily demonstrated in the aortic lesions by the improved starch-gelatin modification of the Warthin-Starry method. They occur in the perivascular lesions, but are particularly likely to be found in the polynuclear infiltrations. They are usually not found in large numbers, but in small groups, in the latent lesions. In the acute exacerbations they may be present in very large numbers, and extending into apparently normal aortic tissue, some distance from the area of infiltration.

#### *Para-aortic Vessels*

A favorite site of predilection for the latent lesions of syphilis are the small blood vessels of the para-aortic tissues. Thickening of the arteriole

walls occurs, often leading to marked sclerosis or to obliteration of the vessel, while active plasma cell and lymphocyte infiltrations occur around the vessels, particularly around the veins. These lesions may be very slight, in some cases they are the only evidences found of a latent syphilitic infection. Usually, however, the process is continuous with that involving the vasa vasorum of the adventitia. In more severe cases the lymphocyte infiltrations are marked, forming irregular cords of cells following the course of the vessels. They extend along the retroperitoneal vessels, and into the root of the mesentery. Spirochetes are found in these infiltrations in very small numbers, it is usually more difficult to demonstrate them in these areas than in the infiltrations extending along the aortic vasa vasorum. Very rarely small milium gummas may develop along the course of these small para-aortic vessels.

#### *Liver*

In both sexes the liver is usually the seat of latent syphilitic lesions. They consist essentially in plasma cell and lymphocyte infiltrations of the periportal tissue, leading eventually to fibrosis and a certain degree of chronic hepatitis. All stages of severity exist, from the mildest to the most severe forms of cirrhosis (*hepar lobatum*). The frequency of occurrence of a mild grade of atrophic hepatitis in latent syphilitics is very high, as is also that of *hepar lobatum*. The latter condition, in my experience, is much more frequent in women than in men. The percentage of liver involvement in my material appears to be on the increase,

particularly in the cases given a modern treatment with the arsenicals. In fifteen successive necropsies on latent syphilitics performed in my laboratory during the last year there was found a chronic diffuse hepatitis, varying in degree from an early mild form to that of an advanced severe atrophic cirrhosis. The relation of this condition to the treatment rather than to the syphilis remains to be determined. It is probable that the diffuse forms of hepatitis are due to something else than the syphilitic infection, as the syphilitic forms of hepatitis are usually irregular and localized, instead of being diffuse. In the average case the liver presents grossly the picture of brown atrophy and chronic passive congestion, with slight or marked irregularity of the surface. In some cases the small periportal infiltrations occur in livers that otherwise appear perfectly normal. The demonstration of spirochetes in the hepatic lesions is more difficult and unsatisfactory than in the case of any other organ. They are found usually only in the most active areas of infiltration, and then in small numbers. Throughout the newly formed connective tissue they are not present, or at least cannot be demonstrated.

#### *Pancreas*

Lesions of latent syphilis are common in this organ, in the form of an interstitial pancreatitis not arising from the pancreatic ducts. In the great majority of cases the process is very mild. The interlobular stroma is increased, edematous, and infiltrated with small collections of plasma cells and lymphocytes. The intralobular stroma is increased, the vessel walls are thickened,

and the islands may become fibroid. This lesion may be associated with diabetes, and has been the most common form of pancreatic disease seen in our diabetic material. I believe, therefore, that syphilitic pancreatitis may be one cause of pancreatic insufficiency, although not the only cause. In the severe forms the organ is small, and much firmer than normal, except in cases in which there is marked edema of the interlobular stroma, in which cases the organ may be larger and softer. Syphilitic pancreatitis is frequently of congenital origin, and may cause pancreatic insufficiency early in life. We have seen two cases of diffuse pancreatic fibrosis in congenital syphilitics with enormous numbers of spirochetes present in all parts of the gland. In the older milder cases the spirochetes are more difficult of demonstration, because, as a rule, they are few in number, and sharply localized in the active plasma cell infiltrations. They occur singly or in small groups. In a case of very active diffuse interstitial myocarditis occurring in a young man of 24 the pancreas showed large areas of infiltration, associated with the occurrence of aggregations of plasma cells and lymphocytes large enough to be regarded as miliary gummas.

#### *Adrenals*

In latent syphilis these organs show almost constantly active infiltrations of plasma cells and lymphocytes varying in size and number from a few small infiltrations scattered through cortex and medulla, up to diffuse infiltrations of marked degree, with interstitial fibrosis and paren-

chymatous atrophy, and thickening of the capsule. These lesions are more frequent and more severe in women than in men. While in the average case of latent syphilis these lesions are not severe enough to produce any clinical disturbances referable to the adrenals yet they may be severe enough to cause marked atrophy and fibrosis of these organs, with a typical picture clinically of Addison's disease. I have seen several such cases, and in my opinion the cases reported in the literature as Addison's disease due to atrophy of the adrenals are probably all of them due to syphilis. There has been an increasing number of such cases reported. Further, I believe that milder degrees of adrenal syphilis may be recognized clinically as a distinct syndrome consisting of low blood pressure, asthenia, irregular patches of pigmentation not marked enough to be regarded as typical of Addison's disease, and accompanied by more or less constant pain in the lumbar region. As has been shown, these cases respond to antisyphilitic treatment, with cure or great improvement in the symptoms. These cases of adrenal syphilis showing a syndrome which might be characterized as sub-Addisonian are probably fairly common among latent syphilitics. Spirochetes are easily demonstrated in the cellular infiltrations, but are usually present in small numbers.

#### *Testis*

The testis of every latent syphilitic shows sooner or later a patchy interstitial orchitis, with atrophy of the germinal epithelium and hyaline fibro-

sis of the basement membrane of the tubules. The process is usually slow and prolonged over a number of years, but is progressive in character, and ultimately the entire organ may become atrophic and hyaline. It preserves its normal size and consistency, however, in spite of the most marked change. An early loss of spermatogenic function occurs in the majority of those who have had syphilis. Owing to its patchy character and the involvement of individual lobules some sperm may continue to be produced by lobules which are not involved in the process. The interstitial cells usually appear hyperplastic and show a brown pigmentation. In spite of this hyperplasia there is generally a loss or reduction in sexual desire and potency on the part of the latent syphilitic. Spirochetes are found in the intertubular-cellular infiltrations that are present in the earlier course of the process. They have been found even in the lumen of the tubules and in the hyaline stroma of the basement membrane. They are numerous in the earlier stages, but are extremely difficult to demonstrate in the later atrophic stages.

#### *Ovary*

I have never found a syphilitic lesion in the ovary, or, at least, any lesion that I could convince myself was due to syphilis. Spirochetes are common in this organ in congenital syphilis, but have never been found in it in acquired syphilis. This organ appears to be immune to the spirochetes, if not absolutely immune, it at least possesses a very high degree of relative immunity.

#### *Tubes.*

The same thing is true of the tubes. They appear to possess a high degree of immunity to the localization or action of the spirochete. I have never seen any lesions in the tubes of the latent syphilitic woman that I could feel convinced were syphilitic in nature, and I have never found any spirochetes in the tubes in acquired syphilis. As is true of the ovary, spirochetes are abundant in the tubes of the syphilitic newborn.

#### *Uterus*

Syphilis of the uterus is by no means rare, both in the primary and in the later stages of the infection. In only a few cases in the latent syphilitic woman have I observed typical syphilitic lesions in the endometrium and extending into the uterine wall, along its smaller blood vessels. There were characteristic perivascular plasma cell and lymphocyte infiltrations, as found elsewhere in the body. Spirochetes were present in small numbers.

#### *Lymph Nodes*

Latent syphilitic lesions are commonly present in the form of a chronic lymphadenitis which is essentially vascular or perivascular in character. It can usually be recognized histologically only when the process is marked. In such cases spirochetes are fairly abundant.

#### *Lungs*

Consideration of this organ has been reserved to the last because of the uncertainty of diagnosis of pulmonary latent syphilis. It is true that the latent syphilitic presents a very high percentage of pulmonary fibrosis and chronic passive congestion (indura-

tion) Localized patches of fibrosis, usually regarded as chronic bronchopneumonia, are extremely common in the lungs of latent syphilitics, but unless there is a gumma present in association, it is practically impossible to diagnose these fibroses as syphilitic in nature. The infiltrations are less perivascular and show fewer plasma cells than those in other organs, and the fibrosis predominates. The demonstration of the spirochete is the deciding criterion of pulmonary syphilis, and in the usual necropsy case of latent syphilis this is practically impossible. I have seen not more than fifteen cases in which the presence of pulmonary syphilis was positively proved. The majority of these cases were associated with gummatous lesions, in the others the process was essentially a disease of the pulmonary arteries (cases of Ayerza's disease). Spirochetes have been demonstrated in the vessel walls of such lungs.

#### SUMMARY

It will be seen from the preceding descriptions that the lesion of latent syphilis repeats the essential pathology of the hard chancre and of the secondary and tertiary lesions of the active stage of syphilis, in that it is predominantly vascular and perivascular, and that the infiltrations are derived from the proliferation of cells *in situ*. Each localization of the spirochete leads to the production of what is essentially a miniature chancre. The presence of plasma cells and lymphocytes in the tissues in the form of localized perivascular infiltrations may be taken as the criterion for the presence of *Spirocheta pallida*. The or-

ganisms, therefore, persist in the tissues, producing slight lesions leading eventually to fibrosis and atrophy of the parenchyma. Clinical symptoms will arise only when this atrophy and fibrosis reaches such a degree that functional disturbance results. In the average case in the male this functional inadequacy appears first usually in the cardio-vascular system, and death from latent syphilis is most frequently due to cardiac insufficiency. There are, however, especial organ susceptibilities to the localization of the spirochete: in one individual the central nervous system, in another the liver, in a third the adrenals, etc., may bear the brunt of the latent infection, so that the clinical picture and the manner of death may vary greatly, according to the organ or tissue chiefly involved.

I have never seen at necropsy a case of perfectly healed syphilis. Search, often prolonged, always reveals active latent lesions in aorta, heart, or other organ. This is as true of cases treated in the modern manner as it is of cases treated with the old mercurial method. If any difference results in the two methods of treatment it would appear to be in the more frequent occurrence of chronic hepatitis in cases treated by the arsenical method. What the treatment accomplishes in either case is the more rapid reduction of the average active case to a stage of latency. There is no evidence pathologically that the case of syphilis ever becomes wholly free from spirochetes. The latency of the infection may last throughout the individual's life, or at any time exacerbations may take place, and the disease arise above the clinical



horizon. What determines these renewals of virulence on the part of the spirochete, whether it be due to a changed quality on the part of the organism or to changes in the resistance of the body, we do not know. The possibility of such a clinical renewal of activity on the part of the spirochaete is always a possibility hanging over the head of the individual who once acquires this infection. Even if the disease never again produces a clinical outbreak, the relatively immune syphilitic will nevertheless develop various functional inadequacies as the price of the latency of his infection. These minute local infiltrations of plasma cells and lymphocytes represent the processes of a local tissue im-

munity. With time this immunity mechanism in itself becomes dangerous to the individual through the functional inadequacies which it may eventually produce. Whether a consistent five-year period of treatment would finally rid the body entirely of spirochaetes I cannot say, for in my material there have been no cases that have been under continuous treatment for that period of time. The fact remains, however, that in syphilitics accorded what has been regarded by the clinician as thoroughly satisfactory treatment, with complete clinical cure, latent lesions of syphilis still present themselves on microscopical examination of the necropsy material derived from such cases.

## Abstracts

*The Modifying Influence of Dichloroethyl Sulphide on the Induction of Tumors in Mice by Tar* By I Berenblum (Jour of Pathol and Bacteriol, Vol XXXII, 1929, p 425)

Three groups of mice, 40 mice in each, were treated in the following manner. One group received applications of tar containing 0.1 per cent mustard gas, on a small area of skin at about the middle of the back (tar plus mustard gas series). The other two groups acted as controls, one receiving applications to tar alone (tar control series), and the other 0.1 per cent solution of mustard gas in acetone alone (mustard gas control series). The applications were repeated on an average once a week. Previous to each application, the hair of the part was cut as short as possible with curved scissors, thus obviating the use of a chemical epilator with its consequent irritation of the skin. After a few weeks the hair ceased to grow in most of all three groups. The experiment was continued until all the animals had died, i.e., for a period of 50 weeks. Five mice in the mustard gas controls survived for 56 weeks from the commencement of the experiment, but the treatment with mustard gas was not continued beyond the 50th week. A few mice which developed large malignant tumors, and which appeared to be suffering, were killed, otherwise the treatment was continued until each animal had died in turn. Sections of the tumors were examined microscopically, and only those showing involvement of muscle, or secondary deposits (one case only) were counted as malignant. The original purpose of subjecting skin to repeated applications of mustard gas and tar was to induce an increase in the blood supply of the skin by means of the mustard gas, and to see how this would influence the induction of tumors as the result of the tarring. It was realized from the beginning that hyper-

emia was not the only change induced by the mustard gas. But finding that the mustard gas itself was not able to induce tumors when applied repeatedly to the skin, and seeing that the hyperemia appeared to be such a prominent factor, it was thought, that if the results fell into line with those of other workers, who used different methods of inducing hyperemia, as section of the sympathetic, such results would then be of value. Repeated tarring in itself leads to a dilation of the cutaneous blood vessels in mice and rabbits, which ultimately developed tumors, but in guinea pigs and rats, which were found to be refractory animals (Itchikawa and Baum). These authors concluded, therefore, that hyperemia must be a primary factor in the induction of tumors. Contradictory results have been obtained as to the effects of hyperemia produced by the removal of the cervical sympathetic ganglia and the induction of tumors by tarring. In the present experiments with the use of mustard gas, an almost complete inhibition of the induction of tumors was observed. The problem of a possible relation between hyperemia and the induction of tumors is therefore no nearer solution by the methods adopted in these investigations. However, the discovery of a substance, which is able to act on an animal so as to make the skin refractory to a carcinogenic tar, is not only of interest in itself, but may be used as an important tool in investigating many problems concerned with the processes underlying the experimental induction of warts. If mustard gas is able to inhibit the induction of warts by tar, the question arises whether this effect is something specific for mustard gas, or whether other irritants may not behave in a similar manner. The possibility of other such substances existing may necessitate a modification of the whole conception of the mixtures of chemical substances label-

led as "non-carcinogenic," because, if a trace of mustard gas, added to a carcinogenic tar, can so mask its carcinogenic effect, other substances capable of acting similarly may occur naturally in such "non-carcinogenic substances." In view of the above observations, one is no longer entitled to assume, if a tar or other mixture of chemical is found unable to produce tumors when painted on susceptible animals, that it contains no carcinogenic principles. One possibility certainly is that no such principle is present, but the other possibility is that, though present, it cannot produce tumors because some other substance is also there which causes the skin to become refractory, as is the case with mustard gas. The author concludes that the addition of 0.1 per cent mustard gas to a carcinogenic tar inhibits the tar from inducing tumors. This anti-carcinogenic effect of mustard gas is due to its action on the animal, so that the skin no longer responds to a carcinogenic tar. The induction of warts is still inhibited if the mustard gas is added to the tar as late as the 11th week of tarring.

*Spectrographic Examination of Pellagrous's Sera* By L. C. Scott, R. H. Turner, and H. S. Mayerson (Proc of the Soc f Exper Biol, October, 1929, p 27)

That exposure to direct sunlight produces or intensifies the erythematous eruptions on the exposed parts of the bodies of pellagrins is an opinion of many observers, the underlying cause of this apparent photo-sensitization is, however, entirely obscure. The auto-experiment of Meyer-Betz with hematoporphyrin and the skin manifestations of hydroa aestivalis, buck wheat disease and other forms of apparent sensitization among the lower animals at least justify the suspicion that some toxic substance is circulating in the blood stream. With the object of determining whether or not the spectrum of pellagrous serum differed materially from that of non-pellagrous, a series of 13 sera was examined with a Hilger quartz spectograph. Each case had been admitted to the New Orleans Charity Hospital, and all were in the acute stage with characteristic eruption, usually with marked oral and gastro-intes-

tinal symptoms. The sera obtained from these patients were examined for the absence or presence of hematoporphyrin, or for any possible differences in the spectrum of the pellagrous serum and that of normal serum. The instruments used were a large E. & Hilger quartz spectograph and a quartz cell measuring  $\frac{3}{4}$ " by  $\frac{3}{4}$ " by  $\frac{1}{8}$ " internal diameter. An arc between two adjustable rods of soft Norwegian iron served as the source of radiation. This arc serves as efficient source not only for the visible but for the ultra-violet part of the spectrum as well. In no instance were the investigators able to detect sufficient difference between the spectra of normal and pellagrous sera to warrant the conclusion that they were not spectroscopically identical. Furthermore, comparison between normal serum containing traces of hematoporphyrin and pellagrous serum left no room for doubt that this substance, at least in any detectable quantity, is not present in the circulating blood of pellagra victims. The examination of the urine from an acute case likewise showed no evidence of the presence of hematoporphyrin in the spectogram.

*A Rapid Precipitation Test for Syphilis* By L. Rosenthal (Proc of the Soc f Exper Biol and Med, October, 1929, p 61)

This test unlike the other existing precipitation tests for syphilis requires no dilution of the serum and antigen, either before or after mixing them. Therefore the test deals with only two ingredients: serum and antigen. The serum is obtained and inactivated in the usual way. As only small amounts of serum are needed, it may be sufficient to secure the blood from the finger. The antigen is prepared by adding 2% solution of cholesterol in acetone to an equal volume of alcoholic beef heart extract, which is obtained by adding 5 cc of 95% alcohol for every gram of beef heart muscle powder from which the ether soluble substances were previously removed by ether extraction. It is advisable to keep in stock separately the alcoholic extract and cholesterol solution, and to prepare mixtures sufficient for only one week's need. If cholesterol crystals precipitate out the solution is placed in an incu-

bator at 37° in order to dissolve them. If a turbidity occurs during the mixing of the cholesterol solution and the alcoholic extract, it is necessary to centrifugalize the mixture and use the supernatant clear fluid. In order to make the final results more conspicuous for reading 0.05 methylene blue powder is added to 10 cc of the cholesterolized antigen. For every test there are needed: 1, A hollow ground slide; 2, two capillary pipettes, one for the serum and the other for the antigen. In order to have the same caliber of the capillary stem for serum and for antigen, both pipettes are drawn from the same piece of tubing. As a standard, pipettes are used which contain 8 drops to 0.1 cc of serum. 3, A glass rod. The technique of the performance of the test is as follows: Four drops of serum are placed in the cavity of the hollow ground slide, and one drop of antigen is floated on the surface of the serum and allowed to stay for 2 minutes. Then the serum and antigen are mixed thoroughly with a glass rod, the slide is gently tilted and rocked for one half minute and then examined. If the room temperature is low it is recommended to use serum and antigen which have been warmed in the incubator at 37° for 15 minutes. It must be borne in mind that the ratio of 4 drops serum to 1 drop antigen in reality constitutes a volumetric ratio of about 8 to 1, inasmuch as the surface tension of the antigen is only one-half of that of the serum. The slide is examined under the low power microscope (magnification 180), the diaphragm being sufficiently narrowed. The reaction is clear cut. In negative sera the whole field is uniformly bluish and has a fine granular appearance without any clumping. This appearance becomes particularly evident when the lens is focused upon the surface layer. In positive sera a definitely marked clumping is observed. The clumps are stained more intensely than the surrounding fluid. Their size varies. Big clumps indicate a strongly positive reaction, clumps of medium size are reported as a positive reaction, and fine delicate clumping is reported as a dubious reaction ( $\pm$ ). The clumping is very characteristic and can be easily distinguished from other particles which may be due to

the impurities of the serum, to the incomplete dispersion of the antigen in the serum, or to the presence of precipitated cholesterol crystals. The test was performed on 1066 sera and checked by the Wassermann reaction. Of 739 that gave a negative Wassermann there were 735 that were negative and 4 positive by the Rosenthal test, of 228 giving a strongly positive Wassermann, 228 gave a positive Rosenthal, of 58 giving a positive Wassermann, 55 were positive by the Rosenthal test and 3 dubious, of 38 dubious by the Wassermann, the Rosenthal gave 19 positive, 17 dubious and 2 negative, of 3 anticomplementary by the Wassermann, the Rosenthal gave 2 negative and 1 positive. There is then an almost perfect agreement of the two tests. In weak positive and dubious Wassermann sera this test gives a more clear cut reaction. Thus, the test combines reliability with technical simplicity.

*Experiences with the Gerson-Diet in Pulmonary Tuberculosis* By Erich Schwalm (Klin Wochschr, October 15, 1929, p 1941)

In the German daily press there have appeared statements that by means of the Gerson diet the severest cases of pulmonary tuberculosis have not only greatly improved but have been practically cured. On the other hand in the scientific tuberculosis literature there has been only unfavorable mention of the method and its results. Schwalm put 20 cases of pulmonary tuberculosis on the Gerson diet in connection with mineralogen and phosphorus cod-liver oil. In some of the cases the use of cod-liver oil was omitted in order to try out more conclusively the effects of the Gerson diet and the mineralogen. As a substitute for the phosphorus cod-liver oil recresal was given. In spite of the fact that there was no difficulty in making the diet palatable, yet in the majority of the patients there arose sooner or later a disinclination, or even a pronounced aversion to the salt free diet. Schwalm regards this as a point of some importance in relation to the use of such a diet for tuberculous patients who frequently suffer from loss of appetite. The mineralo-

gen was always unwillingly taken. From his experience with these 20 cases, the author draws the following conclusions. In no one of the twenty cases of pulmonary tuberculosis treated by the Gerson diet was any improvement of the pulmonary condition noted. In these patients no objective change could be observed, that could be interpreted in the sense of a detoxication or alteration in tone. The weight increase fell within the same limits as occurs ordinarily under Sanatorium treatment. For the increase in weight the phosphorus cod-liver oil appeared to be of the greatest moment, a fact already

known in tuberculosis therapy. No advantage on the part of the Gerson diet could be shown over the usual diet of the German Sanatoria in which the vitamins also play a part. The author closes with the wise remark that in case of a more extensive trial of the Gerson diet, such should be placed in the hands of experienced tuberculosis therapists, who through their many years' experience in the management of large Sanatoria are fitted to make accurate observation and judgment of the results of such treatment.

## Reviews

*Diseases of the Stomach* A Textbook for Practitioners and Students By Max Einhorn, M D, Emeritus Professor of Medicine at the New York Post-Graduate Medical School and Hospital, Consulting Physician to the Lenox Hill Hospital, New York Seventh Revised Edition 593 pages, 131 figures William Wood and Company, New York, 1929 Price in cloth, \$6 00

The first edition of this work appeared in 1896 That this is the seventh shows that it has been of service to the profession in its more than thirty years in which it has been available During this period there has been great progress made in our knowledge of gastro-enterology Particularly has Roentgenology contributed greatly toward a more refined and definite diagnosis in some of the organic diseases of the alimentary tract The author thinks that the especial attention paid to the pathologic conditions of the tract has led to a disregard of neurotic and functional disorders, to the detriment of a host of sufferers In the former editions a prominent place was given to these functional ailments, and in this new edition they are left in the same position of importance While there is much of value contained in this book its background and many of the statements made in it impress the reader as being out of date For instance, the part which constitution plays in gastric disease is not considered and the writer leans to the parasitic theory of cancer etiology Roentgenology receives far too inadequate treatment

*Varicose Veins* With Special Reference to the Injection Treatment By H O McPheeters, M D, F A C S, Director of the Varicose Vein and Ulcer Clinic, Minneapolis General Hospital, Attending Physician New Albany and Fairview Hos-

pitals, Associate Staff of Northwestern Hospital, Minneapolis, Minn 208 pages, illustrated with half-tone and line engravings F A Davis Company, Philadelphia, 1929 Price in cloth, \$3 50

This book is a resumé of a most thorough investigation of the world's literature on the subject of the injection treatment of varicose veins, combined with the care and treatment of approximately 800 cases actually treated at the Out Patient Department of the Minneapolis General Hospital The author has been impressed with the amount of disability that accompanies the extreme and complicated cases of varicose veins, and by the fact that many such patients become invalids for life, when under proper care and treatment they might again be made useful members of society He does not believe that the medical profession as a whole realizes the importance of this condition The time honored and accepted excision of the offending vein, in the hope of cure, has been unsuccessful in such a large percentage of cases that we must seek new and more effective methods of treatment The failure of surgical treatment of varices led the author to adopt the injection method A thorough review of all the methods of injection that have been used is given, the technic is fully and clearly described, as are the complications and sequelae It is a concise and clear statement of the most important facts concerning the injection method

*Clinical Medicine for Nurses* By Paul H Ringer A B, M D, Formerly Chief of Medical Service of the Asheville Mission Hospital, and on Staff of Biltmore Hospital, Biltmore, N C Thrd Revised Edition 330 pages Illustrated F A Davis Company, Philadelphia, 1929 Price in cloth, \$3 00

The first edition appeared in 1918, the

second in 1924. After five years the third is necessary. Since the fundamentals of diagnosis and treatment have changed little in this time, and as conservatism is essential in a book of this kind, not many changes have been made in the material. As the book is one for nurses only, variant views are not emphasized, and as the work is intended solely as a background for teaching purposes, it has been considered wise to rid the book of dogmatic statements in order that the teacher may be able to set forth his own views. The object of these lectures is to place in concrete form a fairly detailed description of the points in the various diseases that nurses will be expected to observe and interpret, and also to form a basis upon which class-room lessons can be assigned and quizzes held, the teacher amplifying as he sees fit. Bacteriology and pathology have been very sketchily traced. The main points dwelt upon have been symptoms and their meaning, complications and their detection, as far as the nurse is concerned. Physical signs have been almost wholly set aside. Treatment is dealt with in a general manner. The book is the first of its kind in the field. It appears to cover the ground intended very thoroughly, and will prove a very useful book for training schools. It may be recommended for this purpose.

*The Female Sex Hormone* Part I Biology, Pharmacology and Chemistry, Part II Clinical Investigations Based on the Female Sex Hormone Blood Test. By Robert T. Frank, A.M., M.D., F.A.C.S., Gynecologist to Mount Sinai Hospital, New York. 321 pages, 86 illustrations and 36 graphs. Charles C. Thomas, Springfield, Illinois, and Baltimore, Maryland, 1929. Price in cloth, \$5.50.

This monograph is based upon twenty-five years of laboratory and clinical research, and embodies and amplifies the material presented in the Charles Sumner Bacon Lectures, at the University of Illinois School of Medicine, 1928. It presents a review of our present knowledge concerning the female sex hormone, and assembles into a comprehensive whole the many fragmentary, yet more or less complementary, reports which

have accumulated. The study of the female sex hormone, which is a growth substance, that has gradually become more and more specialized, until it has developed into the main factor causing "feminineness" in all dimorphous species, has now reached the critical stage in which we may hope at any time to obtain it in pure substance. The sole object of this monograph, the author asserts, is the defense of no thesis, but is the presentation of our present state of knowledge as far as is warranted by the actual proved facts. Unquestionably, modifications in both hypothesis, as well as in theory, will be required. The book performs a distinct service as a compilation of knowledge in this especial field. The literature is quite fully given. It is nicely printed, and well illustrated.

*Atlas of the History of Medicine Anatomy*. By Dr. J. G. DeLint, Lecturer on the History of Medicine at the University of Leyden. With Foreword by Charles Singer. 96 pages, illustrated with 199 Portraits, Views of Anatomical Theatres, Anatomical Drawings, Title-Pages of are Books. Paul B. Hoeber, Inc., New York, 1926. Folio, Cloth, \$6.00 net.

This is a history of Anatomy presented in the form of portraits, reproductions of anatomical drawings, views of the interiors of anatomical theaters, reprints of the title-pages of rare books written by the masters of medicine in the past, arranged in chronological order, and giving the story of the rise and development of anatomical science. With each illustration there is printed a concise description, which assigns the subject its evolutionary position and dates it accurately in its historical sequence. For the understanding of a science it is necessary to understand the history of its development. This is perhaps more obviously true of anatomy than of any other science, for almost the first things a student learns in anatomy are the names of early anatomists. It is fortunate that in anatomy, as in no other science, the names of the great masters and thinkers, who have in their turn, helped to build up the great edifice of anatomical knowledge, should be so inseparably con-

nected with the various parts of the body originally described by them. Anatomical terminology is in itself a perpetual reminder of the scientific achievements of the past. Alas, that modern anatomists have attempted to supplant this picturesque old historical terminology by one that is devoid of any appeal to the imagination. It is necessary to bring medical history to the modern student of medicine in a form quickly and easily assimilable, and this can best be done, as DeLint has done it here, through the medium of illustrations, since most students have learned to take their impressions chiefly through the eye. This method also makes immediately available to the reader material that is inaccessible to the ordinary reader. The perusal of several hundred selected pictures arranged chronologically can give a very good idea of the progress of the knowledge they embody. No demand is made upon the reader's linguistic abilities, and the pictures will appeal to him in that medium through which he is most accustomed to receive impressions. The chief aim of this atlas is to give a picture of the evolution of anatomy from the earliest times to the present day. A classical picture of an anatomical procedure, the portrait of one of the great masters of anatomy, or the title page of one of the great anatomical treatises of the past cannot help but fix the memory of some anatomical discovery. While the chief aim of this work is to aid the study of anatomy, it is hoped that it may find a place in the library of the practitioner who is culturally interested in the history of medicine. It is an atlas that should be in possession of every student of medicine in his freshman year, while engaged in the study of anatomy. Anatomy remains the foundation stone of medicine. It has a long and fascinating history, this atlas will convey to the student something of the truly romantic side of this most important branch of medical study.

*The Medical Museum. Modern Developments, Organization and Technical Methods. Based on a New System of Visual Teaching.* By S. H. Daukes, O.B.E., M.D., D.P.H., D.F.M.&H., Director of

the Wellcome Museum of Medical Science, Affiliated to the Bureau of Scientific Research. An Amplification of a Thesis Read for the Degree of M.D., Cambridge. 172 pages, 44 illustrations. The Wellcome Foundation, Ltd., London, England, 1929.

The experience obtained in organizing and establishing the Wellcome Museum of Medical Science forms the basis upon which this volume has been developed. This experience has demonstrated the practicability and value of such a Museum, which treats of medicine as a whole, and is now regarded as a necessary adjunct to any well-equipped school of medicine. In it are stored, in a condition of preservation more or less effective for teaching purposes, specimens which offer unique material for education and research. Around this center, in the wards, out-patient department and autopsy rooms, revolves a wealth of material illustrating the classic or abnormal manifestations of disease. These manifestations do not necessarily lend themselves to display in a museum jar, indeed, such a jar is too often merely a testimony of failure. As the years pass, there develops an increasing number of ways of depicting the manifestations of a morbid process: the radiograph, electro-cardiograph, the kinematograph, the photograph and painting are all available for making such a complete record of disease. Since more and more instruments have been invented which enable the diagnostician to see into the hidden recesses of the human body—the laryngoscope and ophthalmoscope have been followed by the sigmoidoscope, the cystoscope and many other instruments, by which it has become possible to make exact pictures of conditions which can be rarely seen at the autopsy or in the collections of the Hospital Museum. As a whole the medical museums have not kept pace with these clinical and diagnostic advances, and it is good for us to survey the situation, and to see if, by further development on new lines, we may not provide something of real value for present and future generations. In such an effort has the system described in this volume been conceived, as a form of medical museum which will link up the various branches of medical work into one



demonstration, providing a display which may be fittingly termed *synoptical*. This system is now being developed in the Wellcome Medical Museum, which has been described as the most effective medical museum in the world, in its successful methods of illustrating in the most vivid and instructive way the present state of knowledge of the causation of human disease, and the methods of prevention and treatment. It is both museum and library combined "it is in effect a sumptuously illustrated textbook. In chosen parts of the subject a student may learn more from a quiet hour in one of its divisions than he is likely to gain from any ordinary formal lecture of the schools." This volume outlines the development of the medical museum along synoptical lines, the need for reform and the evolution of the new system. Chapters on general arrangement and classification, etiology, pathology, symptomatology, treatment and prevention are given, with the technical methods employed in the elucidation of these subjects. In numerous appendices are given directions as to building, cases, labels, illustrations, mounting of specimens, methods of preservation, etc. This volume is very timely and should prove most useful to American Medical Schools, in which the synoptical museum is for the greater part unknown and unheard of. Only in McGill and Toronto, on this Continent, has the medical museum been made an active factor in the teaching of medicine. In the United States museum teaching remains almost wholly undeveloped or wholly lifeless.

*The Respiratory Function of the Blood* Part II, Haemoglobin. By Joseph Barcroft, Fellow of King's College, Cambridge. 200 pages, 63 figures. University Press, Cambridge, 1928. Price in cloth 12/6.

The first volume of this series, "Lessons from High Altitudes" was published in 1925. Owing to the rapid advance of knowledge, Professor Barcroft found it impossible to revise his original volume on "The Respiratory Function of the Blood" for a second edition. He has, therefore, decided to break up the work into a series of manageable units, originally intended to correspond more

or less to the "Parts" of the original work. The present volume deals with haemoglobin regarded as a chemical substance. It makes no profession of dealing with the red blood cell, or with the properties of blood. These will form the subject of another volume, so that the consideration of many now classical investigations, such as those of the Rockefeller Institute and the Monogram of Henderson, is reserved for the present. After an introductory chapter, the chapters of this book respectively with porphyrins, haemochrome, cystochrome, specificity of haemoglobin, specific oxygen capacity, manufacture of haemoglobin, nature of haemoglobin solution, molecular weight of haemoglobin, dissociation curve of haemoglobin, theories of the union of oxygen with haemoglobin, kinetics of oxyhaemoglobin in dilute solutions, interaction of carbon monoxide with reduced haemoglobin, effect of temperature on haemoglobin and the biological significance of haemoglobin. For the specialist in the physiology of the blood and for the investigator this volume is indispensable, containing as it does all that is known of haemoglobin from the chemical side.

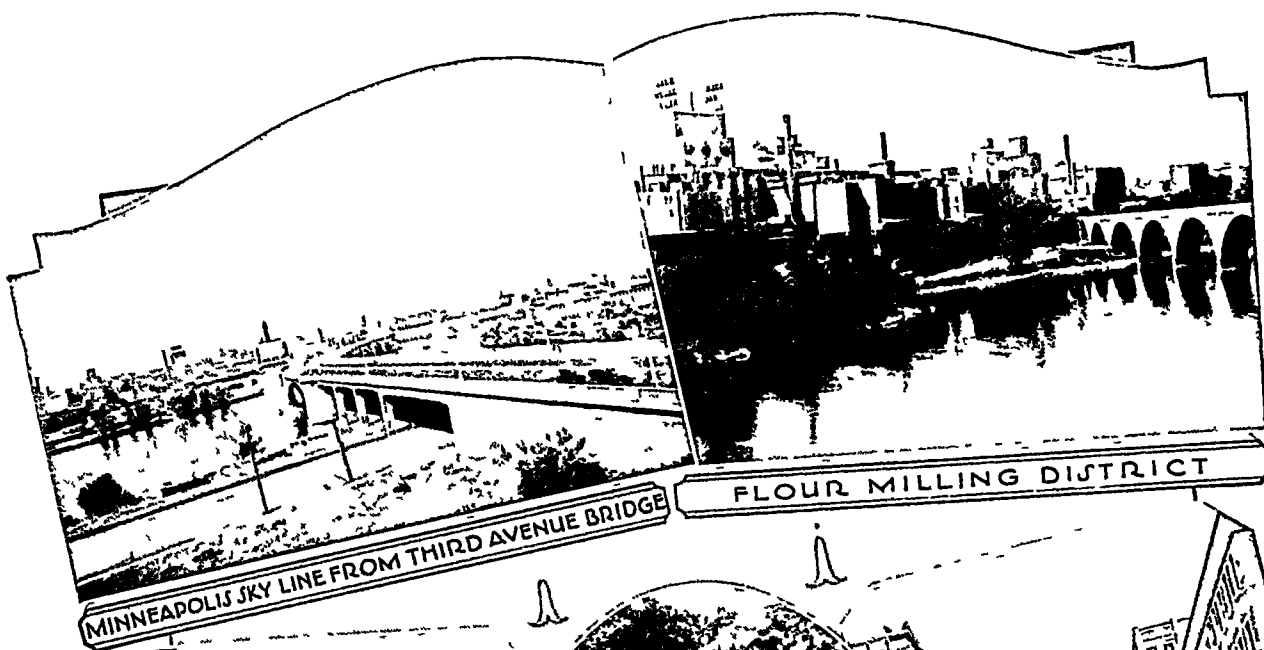
*Health Behavior: A Manual of Graded Standards of Habits, Attitudes and Knowledge Conducive to Health of the Physical Organism, and of Personality, Home, Community and Race.* By Thomas D. Wood, M.D., Professor of Health Education, Teachers College, Columbia University, and Marion Olive Lerrigo, Ph.D., Staff Associate, American Child Health Association. 150 pages. Public School Publishing Company, Bloomington, Illinois, 1927.

This manual has been in preparation by the authors for several years, and is in part an outgrowth of the scale of health habits set up in "Health Education" the report of the Joint Committee on Health Problems in Education of the National Education Association and the American Medical Association. That scale was originally set up by the authors of this Manual, and approved by the Joint Committee and the Technical Committee of Twenty-seven. That scale included only habits, not attitudes or knowledge, and

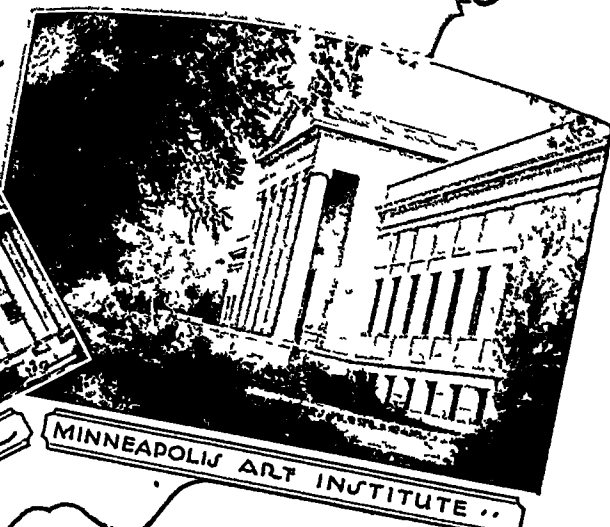
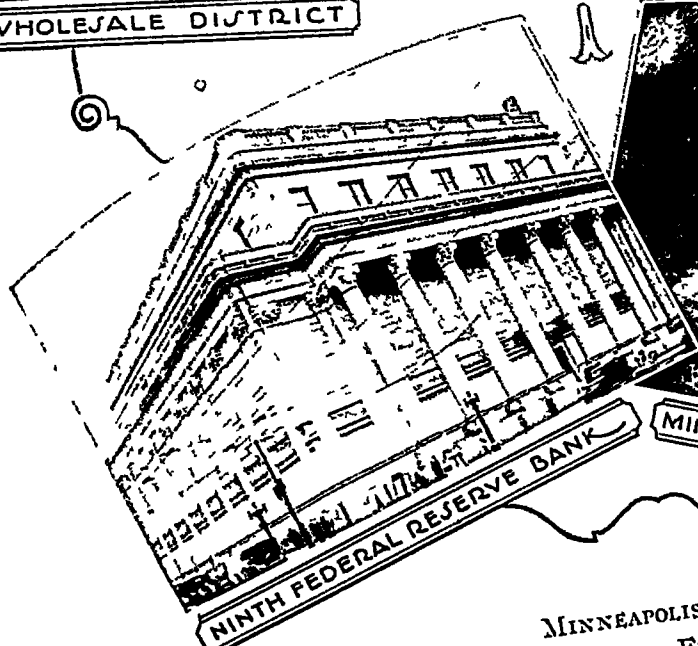
is only for the kindergarten and first three grades. In the present manual the scale of health habits, attitudes and knowledge has been extended to the High School period and early adult life. In a general way the criteria set up in this manual for the different age-period development are extremely good and satisfactory, and the book may well be recommended as a general guide for the intelligent parent in the education and development of the progeny. There is one danger, apparently not recognized by the authors, of too dogmatic and categorical statement regarding such things as diet. The individual peculiarities and idiosyncrasies of human individuals are apparently not considered at all in these scales. For instance, the statement is made that "each person should have one quart of milk daily, drinking a glass at each meal, and getting the rest in the preparation of foods." This is dangerous teaching, for what about the effect of such milk drinking upon a child or person who is sensitized to milk, and to whom milk is actually a poison, producing asthma, urticaria, and a host of severe disturbances. The reviewer is surprised that such an unwise general advocacy of a milk diet escaped the attention of the Joint Committee. This is another example of the danger of too little knowledge on the part of people who set themselves up as able to form general health criteria applicable to all human individuals. Aside from this very serious criticism, the reviewer grants that there is much that is praiseworthy in the conception and practical application of this manual.

*Studies in Nutrition*. An Investigation of the Influence of Saltpeter on the Nutrition and Health of Man with Reference to Its Occurrence in Cured Meats. By Harry S. Grindley and Ward J. MacNeil. Vol. II, Discussion and Interpretation of the Data Relating to the Health and Physical Condition of the Men. With the Assistance of Josephine E. Kerr and William S. Chapin. From the Laboratory of Physiological Chemistry, Department of Animal Husbandry, University of Illinois, 1929.

The manuscript copies of the various chapters of this volume were completed in 1911. The delay in publication has been due to factors beyond the control of the authors. To the careful reader of Volume I and II, it will be evident that there is a distinct conflict between the two joint principal authors of this report. This conflict concerns personal viewpoint, methods of presentation and interpretation of scientific data, and apparently in some instances, even accuracy of record of observations. Perhaps the existence of such a conflict makes for a more reliable report of the investigation. However that may be, it is certain that the great delay in publication is related to it, inasmuch as the author of the present volume has been without authority or responsibility in respect to administrative and financial arrangements. The various positive deductions presented in this volume have been recognized only after diligent search in a somewhat confusing mass of recorded data. The deductions and conclusions of each individual chapter standing as a unit are far less convincing than when those of all the various chapters are considered together. The results of the experiments on bacteria and enzymes support the indication of protective effect of saltpeter in relation to food poisonings, as well as its influence upon the intestinal flora. They also throw a flood of light upon the indication of irritant action of potassium nitrate upon the stomach, and offer a logical explanation of the gastrointestinal irritation, suggested by the blood examination and of renal irritation. In giving prominence to positive findings in a field so controversial, and of such practical importance to particular industries, it has been fully realized that definite and specific points have been presented for discussion, attack and refutation, and that such attacks may be expected. While it is sincerely hoped that any mistakes or false deductions in this work will be exposed and refuted, it is also hoped that such false deductions contained in it may be found to be unimportant.



MINNEHAHA FALLS



MINNEAPOLIS SCENES  
WHERE WE MEET — FEBRUARY 10-14, 1930  
FOURTEENTH ANNUAL CLINICAL SESSION

## College News Notes

The material for the scientific program for the Fourteenth Annual Clinical Session of the College is practically complete. The outline of the five days' program is as follows:

### MONDAY, FEBRUARY 10

Morning	Registration
Afternoon	Opening Session, which will include the addresses of welcome and part of the scientific session
Evening	Scientific Program

### TUESDAY, FEBRUARY 11

Morning	Clinics
Afternoon	Scientific Session
Evening	Scientific Session

### WEDNESDAY, FEBRUARY 12

Morning	Clinics
Afternoon	Scientific Session
Evening	Convocation, followed by Smoker

### THURSDAY, FEBRUARY 13

Morning	Clinics
Afternoon	Scientific Session, short, followed by General Business Meeting at 4 00 o'clock
Evening	Banquet

### FRIDAY, FEBRUARY 14

Morning	Clinics
Afternoon	Scientific Session

The program for the morning sessions in the laboratories and clinics of Minneapolis contains a wealth of material, the outline of which will appear in the final printed program, to be sent to each member of the College. There are, besides the clinics in the University Hospital, the demonstrations in the various laboratories at the University, the clinics in the laboratories and lecture rooms of the Minneapolis General Hospital and of the other hospitals taking part in the clinical program, evidence of a large amount of work of current interest that will be attractive to every member of the College.

In addition to these, one or two items are worthy of especial interest. The first of these are the demonstrations to be given at the Agricultural College of the University. The group of chemists, biologists and nutritional experts on the Agricultural Campus is preparing some demonstrations which would seem at first to the outside the realm of interest of the practicing physician, but the local committee has been astonished and greatly pleased to learn of the many subjects to be presented and the extraordinary interest these

clinics and demonstrations will have for the physician and the scientist. The workers on the Agricultural Campus are manifesting an enthusiastic response to our invitation and will give work of a character which the members of the College will do well to study.

At Glen Lake Sanatorium the Superintendent and staff, together with a large and active consulting staff, are preparing a program of unusual attractiveness and interest. This institution is the Hennepin County Sanatorium for tuberculosis, with over 700 beds, and the spirit of investigation and study is one worthy of attention on the part of the members of the College and their guests. The interest of the staff is not limited to the custodial care of the tuberculous, but includes all the medical problems arising in so large a group of individuals.

In addition to the outline of the program which is attached, papers have been promised by Dr. Allen K. Krause of the Desert Sanatorium, Tucson, Arizona, Dr. Charles A. Elliott of Chicago and Dr. William Gerry Morgan of Washington, D. C. Inasmuch as their formal titles are not as yet at hand, the definite place of each in the daily program is not yet assigned, but the mention of these names is sufficient to call attention to the interest their presentations will have.

The program as outlined is tentative and may be subject to some minor changes.

MONDAY, FEBRUARY 10, 1930

OPENING SESSION, 2 30 O'CLOCK

THE AUDITORIUM

1 Addresses of Welcome

Lotus Delta Coffman, President of University of Minnesota

Elias P. Lyon, Dean of University of Minnesota Medical School

Edward L. Tuohy, Duluth, Minnesota, President of the Minnesota Society of Internal Medicine

J. T. Christison, St. Paul, Minnesota, President of the Minnesota State Medical Association

E. L. Gardner, Minneapolis, President of the Hennepin County Medical Society

2 Reply to Addresses of Welcome

John H. Musser, Jr., New Orleans, President of the American College of Physicians

3 Colloids in Medicine

Ross A. Gortner, Minneapolis

4 Cerebral Localization

Lewis J. Pollock, Chicago

5 The Physiological Panel in Diagnosis and Prognosis

Walter Freeman, Washington, D. C.

6 Gastro-Intestinal Troubles that Now Go Undiagnosed

Walter C. Alvarez, Rochester, Minn.

EVENING SESSION, 8 00 O'CLOCK

THE AUDITORIUM

1 Latent Hyperthyroidism Masked as Heart Disease

Samuel A. Levine, Boston

2 Observations on the Etiology of Gall-Stones

A. C. Ivy, Chicago

3 The Significance of Atelectasis in Bronchopulmonary Conditions

Frederick T. Lord, Boston

4 Moving Pictures of the Results of Stramonium Treatment in Encephalitis

Frederick Epplen, Seattle

TUESDAY, FEBRUARY 11, 1930

AFTERNOON, 2 00 O'CLOCK

THE AUDITORIUM

## VASCULAR DISEASE

- 1 The Effect of Generalized Arteriosclerosis upon the Heart and the Systemic Circulation  
George Fahr, Minneapolis
- 2 Some Newer Aspects in the Problem of Essential Hypertension  
Norman M Keith and James W Kernohan, Rochester, Minn
- 3 The Retinal Vascular Changes in Hypertension  
Henry P Wagner, Rochester, Minn
- 4 Arteriosclerosis in Diabetes  
Elliott P Joslin, Boston
- 5 The Relations of Arterial Sclerosis and Renal Disease  
Alfred Stengel, Philadelphia
- 6 The Causes of Arterial Hypertension  
E T Bell, Minneapolis
- 7 The Management of Hypertension  
James S McLester, Birmingham
- 8 The Use of Nuclear Extractives in Experimental and in Human Anemias  
Noble Wylie Jones, Olaf Larsell and B I Phillips, Portland, Oregon
- 9 The New Possibilities in Classification and Treatment of Anemia  
Hilding Berglund, Minneapolis
- 10 Cinematographic Demonstration of Human Intestinal Protozoa Pictures and  
Remarks on their Biology, Pathology and Treatment  
John V Barrow, Los Angeles

TUESDAY EVENING, 8 00 O'CLOCK

THE AUDITORIUM

- 1 History of Syphilis  
Joseph L Miller, Chicago
- 2 History of Certain Medical Instruments of Precision  
Logan Clendening, St Louis
- 3 Spontaneous Pneumothorax, Non-tuberculous  
F J Hirschboeck, Duluth, Minn
- 4 The Healing of Tuberculosis, Illustrated by Films and Slides  
Francis M Pottenger, Monrovia, Calif

WEDNESDAY, FEBRUARY 12, 1930

AFTERNOON, 2 00 O'CLOCK

THE AUDITORIUM

- 1 Splenic Puncture as a Diagnostic Procedure in Infancy and Childhood  
Julius H Hess, Chicago
- 2 Indications and Technic of Sympathetic Ganglionectomy and Ramisection  
A W Adson, Rochester, Minn
- 3 Results of Sympathectomy in Peripheral Vascular Disease and Scleroderma  
George E Brown, Rochester, Minn
- 4 Sympathectomy in Polyarthritis  
Leonard G Rowntree, Rochester, Minn
- 5 The Relation of Experimental Rheumatoid Inflammation to Allergy  
Benjamin J Clawson, Minneapolis

- 6 Rectal Temperature Curves, Normal and Abnormal  
William B Breed, Boston
- 7 The Limitations of Heliotherapy in Pulmonary Tuberculosis  
Bernard L Wyatt, Tucson, Ariz
- 8 Resumé of Our Present Attitude Regarding Iodine in the Treatment of Toxic Goutre  
James H Means, Boston
- 9 Unusual Addison's Syndromes  
A B Brower, Dayton, Ohio
- 10 A New Method for the Treatment of Pellagra.  
Clyde Brooks, University, Alabama
- 11 Hyperinsulinism and Dysinsulinism  
Seale Harris, Birmingham, Alabama
- 12 In Defense of the Stethoscope  
James B Herrick, Chicago

THURSDAY, FEBRUARY 13, 1930  
AFTERNOON, 2 00 O'CLOCK  
THE AUDITORIUM

- 1 Symposium on The Biology of Cancer  
The Biology of Cancer, from the Experimental Standpoint  
Leo Loeb, St Louis  
The Nature of Heredity in Animals  
H Gideon Wells, Chicago  
Heredity of Cancer in Man  
Aldred Scott Warthin, Ann Arbor  
The Principles of Radiation Treatment  
Francis Carter Wood, New York
- 2 Undulant Fever in California  
J Edward Harbinson, Woodland, Calif
- 3 Undulant Fever, A Clinicopathological Study  
Walter M Simpson, Dayton, Ohio
- 4 Multiple Polyposis of the Colon  
J A Barga, Rochester, Minn

The General Business Meeting of The College will be held at 4 00 o'clock in the Auditorium All Masters and Fellows should attend

FRIDAY, FEBRUARY 14, 1930  
AFTERNOON, 2 00 O'CLOCK  
THE AUDITORIUM

- 1 Symposium on The Rôle of Surgery in Pulmonary Tuberculosis  
Pneumothorax  
James Burns Amberson, Loomis, N Y  
Pneumolysis  
Ralph C Matson, Portland, Oregon  
Multiple Intercostal Neurectomy and Phrenicectomy  
John Alexander, Ann Arbor  
Thoracoplasty  
Philip King Brown, San Francisco  
General Considerations of the Rôle of Surgery in Tuberculosis  
Gerald Webb, Colorado Springs
- 2 Rare Forms of Myelosis  
Hal Downey, Minneapolis





## EXCERPTS FROM MINUTES OF THE MEETING OF THE BOARD OF REGENTS

## AMERICAN COLLEGE OF PHYSICIANS

OCTOBER 27, 1929

The meeting of the Board of Regents was called to order at the College Headquarters in Philadelphia at 9 45 A M, Sunday, October 27, 1929, by President John H Musser, of New Orleans Those present were Drs David Preswick Barr, George E Brown, Arthur R Elliott, Charles G Jennings, Jonathan C Meakins, James Alex Miller, Sydney R Miller, George Morris Piersol, Maurice C Pincoffs, F M Pottenger, Alfred Stengel, Aldred Scott Warthin, S Marx White, President Musser and the Executive Secretary, Mr E R Loveland

After the reading of the Minutes of the previous meeting, President Musser addressed the Board briefly, reporting, "The organization seems to me to be in excellent condition in every way, from the point of view of the type of members coming into the organization and from the point of view also of the excellency of the programs of the last few years and of the program to be put on next year I think a great deal of the credit of this belongs to the two preceding Presidents and to the Regents for their whole-hearted cooperation—also the Governors"

The Executive Secretary reported the following deaths

*Fellows*

Frank C Balderrey	Tucson, Ariz	May 9, 1929
Edgar O Crossman	Washington, D C	June 21, 1929
Daniel Elliott	Newark, N J	
Rudolphus Wm Gelbach	Hoboken, N J	August 2, 1929
Arthur S Loevenhart	Madison, Wis	April 19, 1929
C W McElfresh	Baltimore, Md	
Charles S McVicar	Rochester, Minn	June 29, 1929
John Phillips	Cleveland, Ohio	May 15, 1929
Joseph Wm Rowntree	Waterloo, Iowa	April 3, 1929
C E de M Sajous	Philadelphia, Pa	April 27, 1929
John A Witherspoon	Nashville, Tenn	April 28, 1929

*Associates*

Frank B Granger	Boston, Mass	October, 1928
James W Cokenower	Des Moines, Iowa	April 16, 1929

The following resignations were presented and unanimously accepted on individual resolutions

*Fellows*

James H Dempster	Detroit, Mich
John E Heatley	Oklahoma City, Okla

*Associates*

F J Eichenlaub	Washington, D C
Vincent Fenerty	Philadelphia, Pa
George L Pearson	Youngstown, Ohio

The following gifts to the College Library of publications by members were reported

By Dr George M Albee (Fellow), Worcester, Mass, June 30, 1929

Reprint, "The Care of the Heart in Pneumonia"

By Dr Alexander Bate (Associate), Louisville, Ky, Sept 25, 1929

Reprint, "The Romance of George Rogers Clark and Therese de Leyba"

- By Dr Miles J Breuer (Fellow), Lincoln, Nebr, May 9, 1929  
Reprints, "Case Reports Illustrating Diagnostic Principles in Sexual Psychopathology", August 5, 1929, "A Neglected Focus in Infection," "Suggestions for Effectiveness in Diagnosis"
- By Dr Grafton Tyler Brown (Fellow), Washington, D C, Oct 23, 1929  
Reprint, "Cottonseed and Kapok Sensitization"
- By Dr Ralph O Clock (Fellow), Pearl River, N Y, May 17, 1929  
Reprint, "The Treatment of Burns with Normal Horse Serum"
- By Dr C J Gentzkow (Fellow), Fort Sam Houston, Texas, June 19, 1929  
Reprint, "Insect Pests in Texas"
- By Dr Edwin Henes, Jr (Fellow), Milwaukee, Wis, May 1, 1929  
Book, "Atlanta Proceedings of the Inter-State Postgraduate Medical Association of North America"
- By Dr Dale M King (Fellow), Detroit, Mich, July 5, 1929  
Book, "Why We Are What We Are"
- By Dr Philip B Maltz (Fellow), Washington, D C, June 11, 1929  
Reprint, "Statistical Studies Bearing on Problems in the Classification of Heart Diseases"
- By Dr Aaron E Parsonnet (Fellow), Newark, N J, June 19, 1929  
Reprints, "Physicians' Record System Conducive to Greater Efficiency", "Insulin Treatment of Diabetes Mellitus, Report of Two Cases of Leukemia"
- By Dr Lewis M Silver (Fellow), New York, N Y, June 12, 1929  
Reprint, "The Vanderbilt Clinic—A Retrospect"
- By Dr W Blair Stewart (Fellow), Atlantic City, N J, Sept 28, 1929  
Book, "A Synopsis of the Practice of Medicine"
- By Dr Carl V Vischer (Fellow), Germantown, Philadelphia, Pa, Sept 16, 1929  
Reprint, "Chronic Ulcerative Colitis—Perforation and Peritonitis—Case Report"
- Dr Guy L Connor of Detroit, Michigan, by resolution, was reinstated as a Fellow of the College

The following resolution was regularly adopted

*Resolved*, That the Committee on Constitution and By-Laws shall thoroughly investigate and review the whole situation concerned with those members who were elected to Fellowship some years ago when the initiation fee or annual dues were \$25.00 and \$5.00 respectively, or less, and who subsequently were dropped from the College roll due to the non-payment of higher dues later prescribed

Communications concerning various College activities were read from Dr Walter M Simpson, Dayton, Ohio, Dr Miles J Breuer, Lincoln, Nebraska, and Dr Eben C Hill, Baltimore, Maryland

The Executive Secretary reviewed several communications from Fellows of the College concerning the advisability of maintaining a Placement Service through the columns of *ANNALS OF INTERNAL MEDICINE* and the Executive Offices. On resolution regularly adopted, the Executive Secretary was instructed to work out with the Editor of *ANNALS OF INTERNAL MEDICINE*, a suitable plan of printing announcements concerning positions to be listed through the Placement Service

A letter from Dr Arthur Bullard concerning the progress of the Committee on the Cost of Medical Care was read and briefly discussed. Dr White suggested the possibility of having Dr Ray Lyman Wilbur, Secretary of the Interior, to speak before the Fourteenth Annual Clinical Session, possibly on some subject having to do with medical economics, which would indicate the interest of the College in this subject, since Dr Wilbur is the Chairman of the above mentioned Committee

A resolution was regularly adopted authorizing Dr Wilburt C Davidson, Dean of the Duke University School of Medicine, to have the seal of the American College of Physicians carved on the new Duke Hospital

After receiving the report of the Committee on Credentials through Dr. George Morris Piersol, Chairman, the following physicians were elected to Fellowship

### ELECTED TO FELLOWSHIP

OCTOBER 27, 1929

#### *Arizona*

Russell J Callander, Tucson

#### *Arkansas*

Henry T Smith, McGehee

#### *California*

Andrew Bonthius, Pasadena

J Edward Harbinson, Woodland

#### *Colorado*

James H Brown, Colorado Springs

Harry B McCorkle, Colorado Springs

#### *Delaware*

Olin Sudler Allen, Wilmington

#### *District of Columbia*

Roger M Choisser, Washington

Nelson Gopen, Washington

#### *Florida*

F Clifton Moor, Tallahassee

#### *Illinois*

Charles A Elliott, Chicago

Howard M Jamieson, Decatur

Arthur E Mahle, Chicago

Laurence H Mayers, Chicago

Joseph L Miller, Chicago

Warren F Pearce, Quincy

Sidney A Portis, Chicago

Italo Frederick Volini, Chicago

#### *Indiana*

Harold S Hatch, Indianapolis

#### *Kansas*

Foster L Dennis, Dodge City

#### *Kentucky*

Sydney E Johnson, Louisville

#### *Louisiana*

Harold G F Edwards, Shreveport

#### *Maine*

Mortimore Warren, Portland

#### *Massachusetts*

Francis G Brigham, Boston

Peter A Colberg, Worcester

Maurice Fremont-Smith, Boston

William Mason, Fall River

Hugo A Peterson, Worcester

Lester D Riggs (U S V B ), Rutland Heights

Howard Root, Brookline

Oliver H Stansfield, Worcester

Henry S Wagner, Pocasset

#### *Michigan*

Charles L Brown, Ann Arbor

Trevor G Browne, Battle Creek

Robert A C Wollenberg, Detroit

#### *Minnesota*

Mandred W Comfort, Rochester

Edwin L Gardner, Minneapolis

DeForest R Hastings, Minneapolis

Peter Milton Mattil, Oak Terrace

Lillian L Nye, St Paul

#### *Missouri*

Joseph F Bredeck, St Louis

A Morris Ginsberg, Kansas City

#### *Nebraska*

George W Covey, Lincoln

Harrison A Wigton, Omaha

#### *New Jersey*

Harold S Davidson, Atlantic City

George H Lathrope, Newark

James J McGuire, Trenton

Carlos A Pons, Asbury Park

#### *New York*

Louis Leon Klostermyer, Warsaw

Shailer Upton Lawton, New York

Earl C Waterbury, Newburgh

#### *North Carolina*

James B Bullitt, Chapel Hill

Sylvester D Craig, Winston-Salem

Lewis W Elias, Asheville

Philip W Flagge, High Point

Thurman D Kitchin, Wake Forest

Charles C Orr, Asheville

Paul Henry Ringer, Asheville

James B Sidbury, Wilmington

*Ohio*

Eugen G Reinartz (M C, U S A),  
Dayton

*Oklahoma*

Henry T Ballantine, Muskogee  
Tom Lowry, Oklahoma City

*Oregon*

A H Ross, Eugene

*Pennsylvania*

William Devitt, Allenwood  
George H Hess, Umontown  
Eliah Kaplan, New Castle

*Rhode Island*

William P Buffum, Providence

*South Dakota*

John L Calene, Aberdeen

*Texas*

James E Robinson, Temple  
Samuel E Thompson, Kerrville

John G Young, Dallas

*Utah*

Ralph M Tandowsky, Salt Lake City

*Virginia*

James W Hunter, Jr, Norfolk  
Garnett Nelson, Richmond

*West Virginia*

Oscar B Biern, Huntington  
Milton C Borman, Montgomery  
Adrian H Grigg, Beckley  
Frank C Hodges, Huntington

*Wisconsin*

Karl E Kassowitz, Milwaukee

*Haiti*

Kent C Melhorn, Port au Prince

*Hawaii*

Harry L Arnold, Honolulu

*China*

William W Cadbury, Canton

After thorough discussion, the following resolution was adopted:

*Resolved*, that the Committee on Constitution and By-Laws be requested to enlarge upon the directions dealing with autopsy reports, making the directions more explicit and complete, this Committee to report at a later meeting of the Regents

Dr White, General Chairman of the Fourteenth Annual Clinical Session, at Minneapolis, February 10-14, 1930, gave a detailed report of arrangements for this Session. He suggested that a Friday evening meeting be eliminated due to the train service in Minneapolis. He presented each member of the Board with an outlined program of speakers and topics. He recommended, for the approval of the Board, having the Convocation on Wednesday evening and the Smoker following it.

The Executive Secretary reported upon arrangements for the Minneapolis Clinical Session made through his office. They included reservations for Officers, Regents and Governors at the Curtis Hotel (the Curtis Hotel, though not specified as a headquarters hotel, will be the official hotel for the Boards of the College), reduced railroad fares throughout the United States and Canada on the Certificate Plan of fare and half fare, completion of arrangements for the Commercial Exhibit, consisting of one hundred and four booths with a gross rental amounting to \$11,640.00, other miscellaneous arrangements for the smoother conduct of the business affairs of the College during the Session.

The following recommendation of the Committee on Clinical Session Guests was regularly adopted, after thorough discussion:

*Resolved*, That guests to the Minneapolis Clinical Session shall be admitted according to the following plan:

- (a) Local guests, who are members of the Hennepin and Ramsey County Medical Societies, shall be admitted without any fee, furthermore, they shall be given the opportunity to subscribe to *ANNALS OF INTERNAL MEDICINE* at the rate of \$5.00 per annum for the first year (the period during which the proceedings of the Minneapolis Session will be printed)
- (b) Other visiting guests shall pay a registration fee of \$15.00, and shall be entitled to one year's subscription to *ANNALS OF INTERNAL MEDICINE*, included within

the above fee, any visiting guest who does not desire the Journal, shall pay \$12.00 registration fee

*Committee*

S. MARK WHITE, Chairman

JAMES H. MEANS

JOHN H. MUSSER

SYDNEY R. MILLER

A resolution was regularly adopted requesting Dr. George E. Brown of the Mayo Clinic to prepare a suitable notice for printing in the Clinical Session Program concerning the receiving of guests at the Mayo Clinic during the February Session. Due to the fact that so many of the staff members of the Mayo Clinic will be in attendance at the Minneapolis Clinical Session, it will not be convenient for the Clinic to entertain visitors during that week. Visitors, however, will be welcome at the Mayo Clinic during the days preceding and following the Clinical Session.

Dr. Warthin, Editor of *ANNALS OF INTERNAL MEDICINE*, reported that everything is going very well. The subscription list has increased 50% and the arrangements are very successful. The Journal is being printed long in advance of the date of issue, and is distributed on time.

The following report, comparing volume, circulation and financial data of Volumes I and II of *ANNALS OF INTERNAL MEDICINE*, was presented in mimeographed form by the Executive Secretary to each member of the Board of Regents. He pointed out that Volume II had increased over Volume I by three hundred and sixty-six pages, and that the circulation of Volume II had increased over Volume I somewhat in excess of five hundred. The increased cost of Volume II over Volume I has been due to an increase in the budget for the Editor's office and an increase in the printing cost of the Journal due to its enlarged size. On the other hand, the income has been considerably increased through additional advertising and increased circulation. Although the report shows a small deficit, this will probably be considerably reduced by additional sales of Volume II. Furthermore, the Executive Secretary pointed out that the circulation of Volume III, now in process of publication, has been further increased (October 1929 issue, 2236), and that the volume of advertising is constantly growing, with the result that no further deficits are anticipated.

ANNALS OF INTERNAL MEDICINE  
COST OF ANNALS

	Scientific Matter	Number of Pages News Notes Covers, etc	Paid Advertising	Total
Volume II—July, 1928 to June, 1929	1195	254½	98½	1548
Volume I—July, 1927 to June, 1928	1008	163¼	10¾	1182
Excess pages, Vol II over Vol I	187	91¼	87¾	366*
Circulation, June 30, 1929	2018	Will be increased by future sales **		
Circulation, July 1, 1927	1489	Increased by subsequent sales to date, 1782		
	529	Increased circulation		

EXPENDITURES							
Salaries			\$ 2,693 33				\$ 3,709 88
Equipment, Net							11 10
Postage & Telephone			568 12				684 09
Office Supplies			15 33				104 61
Printing		\$ 9,065 54*				\$11,365 28*	
Less Repayment for excess illustrations	\$481 39			\$261 42			
Less Inventory of stock	497 35	978 74	8,086 80	457 10	718 52		10 646 76
Traveling Expenses							42 50
Miscellaneous (Editor's Office Copyright, etc.)			104 35				127 78
Net Cost			\$11,467 93				\$15,326 72
INCOME							
Subscriptions, segregated from dues at \$6 per member	\$ 8,604 00				\$10,038 00		
Direct Subscriptions	1,441 60				2,168 48		
Gross Receipts	\$10,045 60				\$12,206 48		
Less Expenses	46 00	\$ 9,999 60			37 17	\$12,169 31	
Advertising							
Gross Receipts	\$ 204 22				\$ 2,019 93		
Less Expenses	87 09	117 13			239 59	1,780 34	
Net Income			\$10,116 73				\$13,949 65
Deficit			\$ 1,351 20				\$1,377 07**

\*Printing costs increased due to 366 addition pages (30%) in Volume II

\*\*Deficit on Volume II will be considerably reduced through future orders  
Circulation of Volume III, October number, 2236

The Executive Secretary submitted a report of the work accomplished during the summer months in the Executive Offices, especially the publication of the 1929-30 Directory of the College

The following resolution, looking toward an improvement upon the working out of the present proposal system, was adopted

*Resolved*, That the method of handling proposals of new members shall be changed to the following plan The proposer after filling out the proposal form, signing the blank as proposer and securing the signature of a seconder, shall forward the proposal complete, along with personal letters, to the Governor, Regent or Officer who is acting as endorser, and that said endorser shall forward the entire proposal to the Executive Secretary with his own recommendations There shall be a postal form that the proposer shall mail directly to the Executive Secretary notifying him of the fact that the proposal has been sent to the Governor, Regent or Officer for endorsement This card to enable the Executive Secretary to follow up any proposals that do not come through promptly

The Treasurer's report was submitted as follows

"The Executive Secretary and the Treasurer have not deemed it necessary to make any detailed financial report at this time, since the Annual Audit and Complete Report will be made on December 31, 1929 The Finances of the College are in favorable condition To September 30, 1929, cash receipts since January 1, totaled \$66,725 91, cash disbursements, \$55,871 11, balance, \$10,854 80

Since the last Regents' Meeting at Boston, it has seemed wise to invest some of our surplus in good securities Accordingly, the Treasurer purchased on June 14, 10,000 00 par City of Philadelphia 4½'s at 102¼, or \$10,225 00 On July 24, due to the maturity on August 1 of our 5,000 par Dominion of Canada 5½% bonds, the Treasurer sold same at par, \$5,000 00, and re-invested in 5,000 par, Canadian National Railway 5's at 99¾, or \$4,987 50, the balance on the sale being credited to our bank account

(Signed) CLEMENT R JONES, Treasurer "

This was the first meeting of the Board of Regents since the death of Dr John Phillips in the Cleveland Clinic disaster, last May Dr Phillips had been a member of the Board of Regents and a member of the Executive Committee of the College for several years The Treasurer reported that, on behalf of the College, an appropriate floral tribute had been sent to the Phillips home preceding Dr Phillips funeral The Secretary General reported that an appropriate obituary card had been sent to Mrs Phillips

After some discussion of ways and means, the following resolution was adopted

*Resolved*, That the College shall grant a sum of money each year to be known as the John Phillips Memorial Fund and to be awarded for some outstanding piece of work in the United States or Canada, *Resolved*, further, that a Committee be appointed to formulate plans in detail and to recommend the amount of the Fund

President Musser appointed the following committee to carry out the provisions of the above resolution

DR GEORGE E BROWN, Chairman  
DR ALFRED STENGEL  
DR ARTHUR R ELLIOTT

Due to the vacancy caused on the Board of Regents by Dr Phillips' death, and in accordance with the provisions of the By-Laws, the following resolution was adopted providing for his successor

*Resolved*, That Dr James B Herrick, Chicago, shall be and herewith is appointed a member of the Board of Regents, filling the vacancy caused by the death of Dr John Phillips, until the next regular election at the Minneapolis Session

The following Committee was appointed by the President to serve until the Board of Governors has elected successors thereto

COMMITTEE ON CREDENTIALS FOR ASSOCIATION

Edgerton L Crispin, Los Angeles, Calif (Chairman)  
Charles H Cocke, Asheville, N C  
Allen A Jones, Buffalo, N Y  
D Sclater Lewis, Montreal, Quebec

The Board of Regents authorized a meeting of the Committees on Credentials early in January, in order that all proposals may be examined and recommendations prepared in advance of the Minneapolis Clinical Session In accordance with the provisions of the By-Laws, no proposals will be acted upon preceding the Minneapolis Clinical Sessions unless filed before January 10, 1930 The Committee on Credentials, however, strongly recommends that all proposals be filed before the end of December, 1929

E R LOVELAND, Executive Secretary



Dr John F W Meagher (Fellow), Brooklyn, is author of a book, "Masturbation and the Psychosexual Life," recently published by William Wood and Company

The American Gastro-enterological Association has as its officers many members of the American College of Physicians Dr Frank Smithies (Master), Chicago, is President, Dr Clement R Jones (Fellow), Pittsburgh, is Second Vice President, Dr Charles G Lucas (Fellow), Louisville, is Secretary, Dr Thomas Wray Grayson (Fellow), Pittsburgh, is Treasurer, Dr George Morris Piersol (Fellow), Philadelphia, Dr Franklin W White (Fellow), Boston and Dr Walter C Alvarez (Fellow), Rochester, are members of the Council, Dr Harlow Brooks (Fellow), New York, Dr Allen A Jones (Fellow), Buffalo, and Dr Louis M Gompertz (Associate), New Haven, constitute the Committee on Admissions and Ethics

Dr Hugh S Cumming (Fellow), Surgeon General of the U S Public Health Service, Washington, D C, is one of the incorporators of the National Institute of Psychology The active members are made up of about fifty experimental psychologists, and their avowed purpose is to conduct a national laboratory for psychologic research "similar in some of its functions to the Bureau of Standards, but not under federal control"

Dr Everett G Geer (Fellow), St Paul, addressed the Minneapolis Academy of Medicine, October 9, at the Town and Country Club on "Evulsion of the Phrenic Nerve for Pulmonary Tuberculosis"

Dr George H Whipple (Fellow), Professor of Pathology and Dean of the University of Rochester School of Medicine, assisted in the conduct of a symposium on anemia before the Section on Medicine of the New York Academy on Medicine on October 15

Dr Vernon C Rowland (Fellow), Cleveland, addressed the Academy of Medicine of Cleveland, October 18, on "Present Status of the Periodic Health Examination"

Dr E Roland Snader, Jr, (Fellow), Philadelphia, is author of an article, "A Modern Conception of Treatment of Cardiovascular Syphilis," which appeared in the September Issue of the Hahnemannian Monthly

Dr Lewellys F Barker (Fellow), Baltimore, conducted two Clinics on October 31 and November 7 under the auspices of the Division of Medical Extension of the University of Maryland Invitations and cards of admission were issued to various physicians of Maryland and surrounding territory by the President of the University and the medical faculty

Dr D N Silverman (Fellow), New Orleans, Associate Professor of Gastro-enterology in the Graduate School of Medicine of The Tulane University of Louisiana, addressed the South Texas District Medical Society at Houston, Texas, October 11, 1929, on "Chronic Ulcerative Colitis"

Dr Sydney R Miller (Fellow and President-Elect of the American College of Physicians), Baltimore, addressed the American Academy of Periodontology in Washington, D C, October 10, on "The Value of Blood Chemistry in Periodontology" On October 18, he attended the meeting of the East Tennessee Medical Society, speaking on "The Maltreated Malnourished, Nervous Patient" As Councillor from the State of Maryland, he will attend the meeting of the Southern Medical Association in Miami in November, presenting before the Medical Section in Collaboration with Dr Charles A Waters (Fellow), Baltimore, a paper on "The Clinical and Roentgenological Value of Intravenous Cholecystography," illustrated by moving pictures

Dr E J G Beardsley (Fellow), Philadelphia, addressed the Cumberland Valley Medical Association at Carlisle, Pa, on September 26, 1929 The subject was "The Common Psycho-neuroses of Every Day Practice"

Dr E Roland Snader, Jr (Fellow), Philadelphia, is Vice President of the Eastern Homeopathic Medical Association, which held its Eighth Annual Convention at Wilmington, Delaware, on October 23, 24, 25 and 26

The following Fellows of the College were represented on the program of the Eighth Annual Convention of the Eastern Homeopathic Medical Association at Wilmington, Delaware, on October 23, 24, 25 and 26 by the following papers

Dr G Harlan Wells, Philadelphia, "Relative Efficiency and Stability of the Various Preparations of Digitalis"

Dr Donald R Ferguson, Philadelphia, "Problems in Diabetes"

Dr G Morris Golden, Philadelphia, "Auscultatory Percussion—its Value as a Diagnostic Measure"

Dr E Roland Snader, Jr, Philadelphia, "The Cardio-vascular Phenomena of the Menopause"

Dr Joseph McFarland (Fellow), Philadelphia, addressed the Pathological Society of Philadelphia on October 10, his subject being "The New Bureau for the Study of Tumors"

Dr William L Rich (Fellow), Salt Lake City, and Dr Maurice M Critchlow (Fellow), Salt Lake City, were elected President-Elect and Secretary, respectively, of the Utah State Medical Association at the last annual meeting during July

Dr Howard R Hartman (Fellow), Rochester, Minnesota, was one of the principal speakers at a graduate course arranged by the Utah State Medical Association at the Salt Lake General Hospital during September

Dr Wilburt C Davidson (Fellow), Dean of Duke University School of Medicine, Durham, N C, extended greetings to the University of Virginia Medical School at the dedication of its new \$1,400,000 group of medical buildings, on October 22, during the annual meeting of the Virginia State Medical Society

Dr John Dudley Dunham (Fellow), of Columbus, Ohio, has been appointed consultant in Internal Medicine to the Student Medical Service of Ohio State University

Dr Crawford R Green (Fellow), Troy, N Y, addressed the Rensselaer County Medical Society, Troy, N Y, Nov 12 on "The Symptoms and Signs of Pneumonia"

Dr David Riesman (Fellow), Philadelphia, Pa, will address the Atlantic County Medical Society, Atlantic City, N J, on November 22 1929 His subject will be "Diagnosis and Treatment of Nephritis and Nephrosis"

Dr Harold S Davidson (Fellow), Atlantic City, N J, has been elected Vice President of the Atlantic County (N J) Medical Society

Dr Thomas F Reilly (Fellow) of New York delivered a lecture to the Academy of Medicine of Newark, N J, Thursday night, November 21, 1929, on "Headache"

Dr Andrew Conrad Ivy (Fellow) gave an address on "The Newer Physiology of the Gall-Bladder," at the meeting of the International Postgraduate Assembly, in Detroit, October 25th

At the same meeting of the International Postgraduate Assembly in Detroit, October 25, 1929, papers were read by Harlow Brooks (Fellow), New York, and Aldred Scott Warthin (Master), Ann Arbor

On November 27, Dr Aldred Scott Warthin (Master), addressed the Buffalo Academy of Medicine on "The Lesions of Latent Syphilis" Previous to the meeting, a large dinner was given Dr Warthin, by Dr C W Greene (Fellow) of Buffalo, at the Saturn Club

George C Hale (Fellow), Dean and Professor of Medicine, University of Western Ontario, London, Ontario, gave a diagnostic clinic on "Cardiovascular-renal Problems," at the Highland Park General Hospital, December 5, 1929

Dr Charles Jennings (Fellow), of Detroit, gave an address on "Pneumonia" before the St Clair County Medical Society, on November 21, at Port Huron, Michigan

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Dr Paul Roth (Fellow), of Battle Creek, Michigan, is the author of a paper on "Physiotherapy," in the December number of the Journal of the Michigan State Medical Society, for December, 1929

Dr W H Marshall (Fellow), of Flint, Michigan, has a paper on "Medicinal Therapeutics" in the Journal of the Michigan State Medical Society, for December, 1929

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Dr Charles E Stewart (Fellow), of Battle Creek, Michigan, has a paper on "Practical Dietetics in the Light of Modern Scientific Research," in the Journal of the Michigan State Medical Society, for December, 1929

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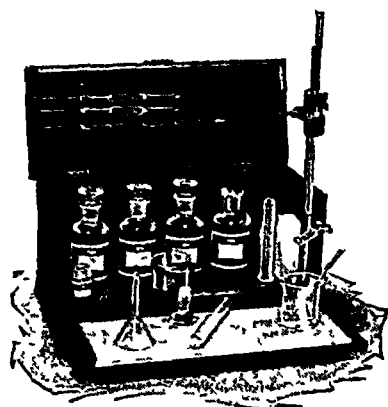
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|----------------------------------|---------------------------------|
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| Walter C Alvarez, Rochester      | Elliott P Joslin, Boston        |
| James Burns Amberson, Loomis     | Norman M Keith, Rochester       |
| J A Bagen, Rochester             | James W Kernohan, Rochester     |
| John V Barrow, Los Angeles       | Olaf Larsell, Portland          |
| E T Bell, Minneapolis            | Samuel A Levine, Boston         |
| Hilding Berglund, Minneapolis    | Leo Loeb, St Louis              |
| William B Breed, Boston          | Frederick T Lord, Boston        |
| Clyde Brooks, University, Ala    | Elias P Lyon, Minneapolis       |
| A B Brower, Dayton               | Ralph C Matson, Portland        |
| George E Brown, Rochester        | James S McLester, Birmingham    |
| Philip King Brown, San Francisco | James H Means, Boston           |
| J T Christison, St Paul          | Joseph L Miller, Chicago        |
| Benjamin J Clawson, Minneapolis  | John H Musser, New Orleans      |
| Logan Clendinning, Kansas City   | B I Phillips, Portland          |
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| Hal Downey, Minneapolis          | Francis M Pottenger, Montrovia  |
| Frederick Eppley, Seattle        | Leonard G Rowntree, Rochester   |
| George Fahr, Minneapolis         | Walter M Simpson, Dayton        |
| J Edward Harbison, Woodland      | Alfred Stengel, Philadelphia    |
| A C Ivy, Chicago                 | Edward L Tuohy, Duluth          |
| Walter Freeman, Washington       | Henry P Wagener, Rochester      |
| E L Gardner, Minneapolis         | Aldred Scott Warthin, Ann Arbor |
| Ross A Gortner, Minneapolis      | Gerald Webb, Colorado Springs   |
| Seale Harris, Birmingham         | H Gideon Wells, Chicago         |
| James B Herrick, Chicago         | Francis Carter Wood, New York   |
| Julius H Hess, Chicago           | Bernard L Wyatt, Tucson         |

(Consult Page 635 for details)

NON-MEMBERS OF THE COLLEGE may attend by paying the prescribed registration fee. Consult the Executive Secretary concerning details. RAILROAD TRANSPORTATION has been arranged on the Certificate Plan of REDUCED FARES. HEADQUARTERS Minneapolis Auditorium

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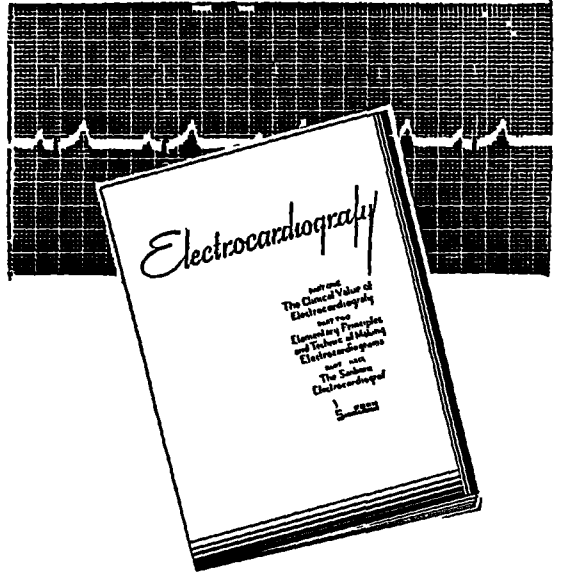
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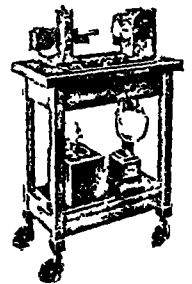


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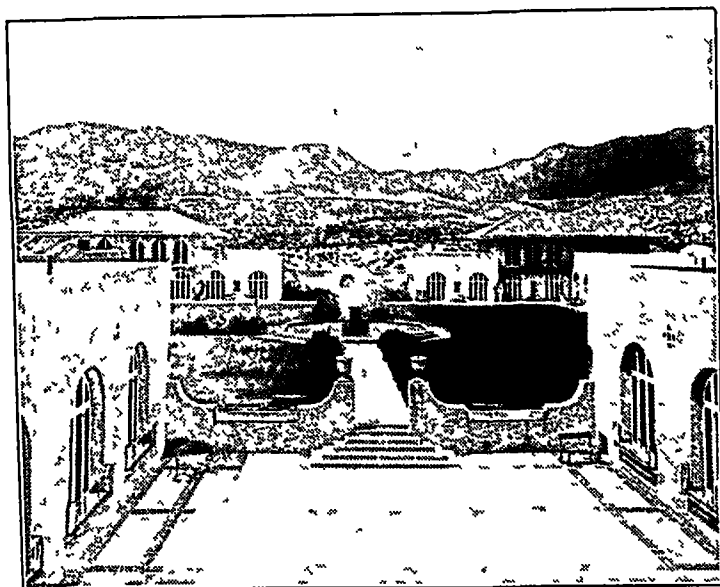
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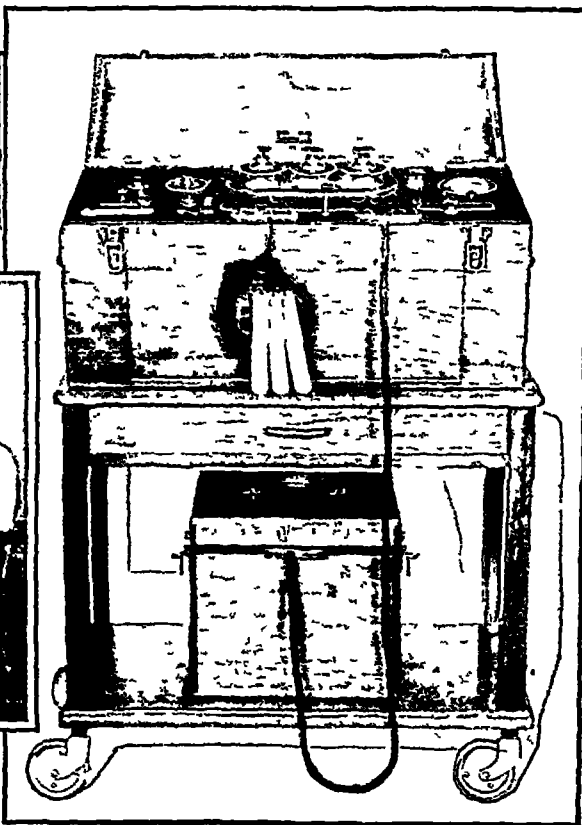
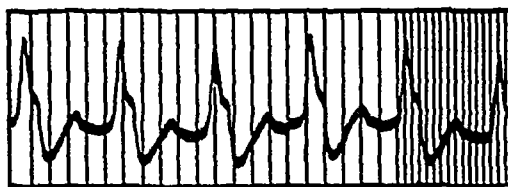


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# The Significance Of Abnormal Metabolic Features In The Management Of Thyrotoxicosis\*

WALTER B PALMER, *New York*

THE management of the thyrotoxicoses is a popular topic for medical meetings and medical journals. During the past few years scores of articles dealing with this phase of the thyroid problem have appeared. Generally the authors are on the defensive, advocating either surgical or medical treatment. At the outset I wish to make it clear that this is not my intention. Many clinicians prefer to postpone surgery until all medical measures have proved of no avail. In some of the hospitals a case of exophthalmic goiter is seldom if ever seen on the medical services, while in others the medical and surgical men work together. At the Presbyterian Hospital, in New York, we have a combined medical and surgical thyroid clinic. All cases with toxic symptoms enter the medical service and the combined group decide as to the course considered best for the individual case. While not all cases are treated surgically, the majority having moderately severe or severe symptoms, provided there is no contraindication, are advised to take the operative course and are prepared for operation on the medical service.

The medical and surgical men meet together in the dispensary for follow-up work, consultations and treatment of the non-operative cases. After several years' experience in the combined clinic certain abnormal metabolic features in the condition appear to need more consideration than they seem to receive generally to the cure of the thyrotoxic, no matter whether surgical or medical.

Since the earliest description of Exophthalmic Goiter by Parry, Graves and Basedow, clinicians have been impressed by the marked loss of weight, weakness and frequent occurrence of troublesome diarrhea. Gradually there have accumulated numerous observations made in the laboratory—nitrogen loss, the difficulty of maintaining nitrogen equilibrium even with high caloric diets, elevated basal metabolism, an upset creatin-creatinin mechanism, inability to store glycogen with the associated alimentary glycosuria, transitory spontaneous glycosuria and occasional development of diabetes mellitus, disturbed fat metabolism reflected in the high cholesterolin and fat contents of the blood, loss of phosphorus and calcium related in all probability to the diminished density of the bones as revealed by X-ray, which indicate a widespread disturbance of

\*Presented at the Boston Meeting of the American College of Physicians, April 11, 1929

metabolism The significance of some of these facts is not clear In the case of others we find valuable aids in the management of the thyrotoxicoses

Probably the most widely employed and useful laboratory aid is the determination of the basal metabolic rate Certainly most will agree that in a majority of instances the degree of elevation is an indication of the severity of disease process and serves as a guide in any particular method of treatment

On the other hand we encounter cases where we must rely on good clinical judgment rather than depend entirely on the results of the basal metabolic determination Two cases may be presented to illustrate this point

A school teacher, thirty-seven years old, having enjoyed good health up to a few months before coming under observation, became weak, nervous, irritable, losing weight in spite of a good appetite, develops exophthalmos, a symmetrically enlarged thyroid gland, tachycardia and tremor She did not benefit by her summer vacation and was unable to take up her teaching in the autumn Her basal metabolic rate was  $+35$  Pulse 100-110 The general appearance was one to suggest a severe Graves' and predict a long protracted course as the result of medical care She was much opposed to surgical interference so that rest in bed for one month combined with radiotherapy for four months was tried out without benefit

As the result of this disappointing trial she consented to a partial thyroidectomy which was carried out with

marked immediate improvement After four months' rest she resumed her usual teaching schedule without difficulty and has remained at her work for a year and a half

Contrast this case with the second, a laboratory technician of 30, who began to lose weight, became nervous, weak, tiring easily, sleepless, complaining of palpitation, during a period of four months before seen She was a small, thin girl with no exophthalmos, only a slightly enlarged gland, marked tremor, hot moist skin, pulse rate of 100-110, and a basal rate of  $+40$  After two months' rest she was markedly improved, gained in weight, pulse 80-88, a slight tremor and the basal rate had come down to  $+20$  She resumed work in the laboratory where she has been for nearly a year She has from time to time taken a little Lugol's solution It is true she may have a remission more serious than the initial attack

The two cases were alike in several respects The basal metabolic rates were approximately the same,  $+35$  and  $+40$ , the pulse rates the same, duration of the symptoms the same, yet the disease clinically seemed more severe in the first case than the second Nervousness and weakness were more marked, the first girl could not carry on and the second could It was not the basal metabolic rate which determined the course followed in treatment but the clinical condition

Cases could be multiplied demonstrating the discrepancy between the clinical condition and the elevation of basal metabolism There are those with a high basal who carry on their daily activities without difficulty and

apparent damage to their circulatory system, others who with a normal basal are invalids and develop cardiac failure. Illustrations are to be found in all groups no matter the type of treatment. I have been impressed with the occurrence of very high basal rates (+60 to +80) in some of the cases of secondary Graves' (toxic adenoma) with only mild toxic symptoms clinically. These cases usually withstand operations well while in some of the younger primary Graves' cases with basal rates between +40 and +50 the toxic manifestations clinically are severe and frequently cause much concern and worry post operatively.

The value of iodine in preparation for operation is now too well known to need comment. The reduction of the basal together with amelioration of symptoms is most striking after the administration of small amounts of iodine. The optimum effect usually occurs in from one to three weeks. Smith has observed that patients not under the full effect of iodine have a more labile basal metabolic rate than those where the effect is optimum. News of the impending operation causes the basal metabolic rate to rise markedly in the first instance while if the iodine has produced its maximum effect the basal is unchanged when surgical measures are discussed. It is suggested that this procedure may be employed to determine whether the optimum effect of iodine has been reached. Such a procedure is time consuming but may be serviceable in doubtful cases.

The difficulty in establishing nitrogen equilibrium, first observed by

Friederick Muller, is, I believe, of considerable importance in the dietary control of patients with thyrotoxicosis. A great deal has been said about the use of a high caloric diet but too frequently not sufficient attention is devoted to its accomplishment. In connection with studies to be mentioned later I have had occasion to follow the nitrogen balance in several of our cases. It was found, as Sturgis<sup>1</sup> points out, that in the more toxic cases a caloric intake of 75%, to 100%, above the actually determined basal with the patient in bed, was necessary to establish nitrogen equilibrium or a positive balance. In a few instances more than 100% was required. In others, however, 50% above the basal was sufficient to maintain nitrogen equilibrium and a constant or slight gain in weight. There is a variation among patients in this respects which is difficult to explain. It does not necessarily hold that the higher the basal the larger the percentage over the actual basal in caloric intake is required to maintain nitrogen equilibrium. An important factor appears to be the clinical evidence of toxicity. In my opinion every effort should be made to give sufficient food to produce a gain in weight. A little special attention to the diet can usually bring this about. We are all familiar with the surgical disasters in the emaciated patient who is operated on when losing weight. In cases treated by X-ray or rest alone an adequate diet is of equal importance.

Associated with the disturbed nitrogen metabolism is the altered creatin-creatinin mechanism. In normal individuals on a creatin free diet no

creatin appears in the urine. The majority of the thyrotoxicoses excrete considerable amounts of creatin. In a study of our 60 cases we have observed the excretion of over one gm of creatin in 24<sup>h</sup> in several instances. Associated with the appearance of creatin is a lowered creatinin excretion. Usually the daily excretion of creatinin nitrogen is 7-11 mgms per kilo, in the cases of exophthalmic goiter it is only 3-6 mgms. Prolonged feeding with a high caloric low protein diet will cause creatin to disappear from the urine. We have observed that from three to five days after the administration of iodine there is a spectacular decrease in the amount of creatin excreted, to either insignificant amounts or none at all.<sup>2</sup> No commensurate increase in the creatinin occurs. This effect of iodine on the creatin output does not seem to be necessarily dependent on the drop in the basal rate, for in some of our cases we have seen striking drops in the creatin with no change in the basal rate. In view of the suspected importance in normal metabolic function of the muscles in relation to creatin and creatinin the possible significance of this fact in the improvement can not be overlooked. After making these observations the discovery by Fiske and Subbarow<sup>3</sup> and almost simultaneously by the two Egglestons<sup>4</sup> in Hill's laboratory, London, of the labile phosphorus-creatin compound increased our interest in the behavior of creatin in toxic goiters. The implication is that the phosphorus-creatin compound plays an important part in the normal function of muscle particularly in its tone and contractibility.

One of the outstanding symptoms of hyperthyroidism is muscular weakness. It is impossible therefore to prevent the imagination from leaping ahead of our facts and wonder if in the thyrotoxicoses there may not be interference with the normal function of this newly discovered phosphorus compound.

Possibly linked with the abnormal creatin behavior is the low creatinin excretion. As you know, creatinin appears in the urine of normal individuals in constant amounts and is believed to be present in proportion to the active protoplasmic mass. So constant is the daily excretion of creatinin that it may serve as a check on the complete collection of 24 hour specimens for it is possible to detect the absence of a single voiding.

The above facts concerning the creatin and creatinin strengthen my belief that attention to the general nutrition is of great importance not only in preparation for operation but for care in general.

Now that the indiscriminate use of iodine in the treatment of thyroid disease of all sorts and descriptions is so prevalent it is rare for a case of Graves' disease to come to the clinic without the story of having taken iodine. Many times this is unfortunate since the strikingly good effect of iodine operatively is lost. In cases such as these the effect of iodine on the creatin excretion may be useful in the pre-operative stage. A case will illustrate the point. A Jewish school girl, 16, ill with Graves' disease for six months. For five months she had been taking iodine daily. At first she improved but for the past

four months no improvement, in fact her nervousness and palpitation have increased, and she has lost weight steadily. On admission there was marked restlessness, a high grade of exophthalmos, a large hard thyroid gland, pulse 140-150, a marked tremor and basal +61%. The iodine was stopped, she was given a creatin free diet of caloric value amounting to 100% in excess of her actual basal. The only drug employed was luminal /03 t i d. Within two weeks the situation was much improved. The gland was smaller and much less hard, the restlessness and tremor less marked and the pulse rate 110-120. She was gaining weight but the basal remained high +67%. She was excreting large amounts of creatin. As it was deemed advisable to remove part of the gland, iodine in the form of Lugol's solution was given in daily doses of 1 cc for 15 days and 3 cc for five days. After eight days the creatin disappeared but at the end of 19 days the basal metabolism was still high +54%. The improvement while taking iodine was definite but not marked. Partial thyroidectomy was done without incident. Similar cases have been observed and the question arises if the disappearance of creatin from the urine may not, in these cases that have received iodine before, serve as an indication of the optimum effect, of subsequent iodine administration.

The deviations from normal in the fat and carbohydrate metabolism are undoubtedly important but our knowledge does not at present permit of any significant practical use of the facts at hand.

Although the utilization of phosphorus and calcium is far from normal as shown by the increased excretion of these elements in thyrotoxic conditions and thyroid extract administration, and reflected in the diminished density of the bones, the clinical significance of these facts is not clear. We have had under observation in our wards for over a year a case of mild hyperthyroidism associated with marked disturbance in bone metabolism. In this particular case, which will be reported in detail by Dr. Turner or Miss Benedict later, the laboratory study of the calcium and phosphorus metabolism seems to have been of distinct service clinically. The patient is an unmarried girl of 19 who entered the Presbyterian Hospital in August, 1927, complaining of weakness in the legs and difficulty in walking. Her family history is good. During childhood she had measles and whooping cough. Influenza in 1918 and again in 1921. Possibly malaria in 1922. Septic sore throat, 1920. Tonsillitis, 1923, although the tonsils had been removed in 1915. She associated the onset of her present illness with the severe sore throat contracted in March, 1923. About a month after the sore throat her knees became stiff and she lost strength. For a few years she wandered from clinic to clinic, physician to physician, consulted osteopaths and chiropractors without relief. The stiffness of the knees and ankles increased, the wrists, elbows, and shoulders became involved. During this period she was treated for arthritis, received thyroid extract, pituitary extract, calcium, phosphorus, at one clinic a high basal (+25%)

was discovered and Lugol's solution was administered, various forms of light therapy, galvanic and faradic currents were employed

On admission she was a poorly developed but fairly well nourished, good natured girl with difficulty of motion in her ankles, knees, wrists and elbows. The flexibility of spine was greatly decreased. She was unable to turn herself in bed. Eyes prominent but not true exophthalmus, thyroid gland not enlarged. No thrill or bruit. All ribs moderately tender on pressure. Heart negative except for over activity and rate varying between 100 and 130. Neither spleen or liver palpable. Marked tremor of the fingers and hyperactive reflexes. Blood and urine normal. Basal metabolic rate varied between +6 and +25%. Wassermann. Alcoholic antigen negative, Cholesterin +. X-ray of the bones revealed marked decalcification of all the bones. The epiphyses of both radii and ulnae ununited with disturbance at the epiphyseal margin. While the changes were suggestive of those seen in osteomalacia Dr. Golden felt they were not entirely characteristic. Furthermore, he noted in the right humerus evidence of periostitis and discovered a few areas suggestive of bone destruction, indicating possibly a lutetic process. Further Wassermanns were taken with varying results—negative at times, + or ++ at others. In view of the apparent derangement of the calcium and phosphorus metabolism she was transferred to the research ward and her Ca—P balances have been followed for over a year. Without subjecting you to the many details of the year's tedious work, the

chief results demonstrate, I think, the importance of the studies in directing treatment. Her blood calcium was a low normal, her blood phosphorus distinctly low, 1 mgm per 100 c.c. It was found that on a regular adequate diet she was constantly in negative phosphorus and calcium balance nor was this influenced by either sunlight or cod liver oil singly or combined, but when cod liver oil and 5 grms of calcium lactate were combined, she immediately established a distinct positive calcium and phosphorus balance. The blood calcium and phosphorus showed no change. There was also slight clinical improvement. Although there was no clinical evidence favoring syphilis the X-ray finding and the equivocal behavior of the Wassermann seem to justify a course of antileutic treatment. The calcium and cod liver oil were stopped and she received several doses of neoarsphenamine and mercury. The Ca—P balance immediately became negative and clinical improvement ceased with no change to be observed in the bones as shown by X-ray. On resuming cod liver oil and calcium by mouth the positive balance was re-established and she seemed to improve clinically, joints were less stiff, she could turn over in bed but there was little change to be noted in the X-rays. For six months she was kept on cod liver oil and calcium lactate with slow but steady improvement clinically and always in positive calcium and phosphorus balance. It was then determined to substitute ergosterol for cod liver oil. For two months this was combined with calcium lactate and two months without calcium. While combined with cal-

cium the effect seemed to be equivalent to the cod liver oil Ca combination, but when the Ca was omitted there was a gradual reduction in the amounts of Ca and P retained. Briefly the result of her year's stay in the hospital has demonstrated the type of treatment which seems most effective. She is now able to walk with some difficulty about the ward, knitting, making baskets and in good nutrition. X-ray of her bones reveals a marked increase in the deposition of calcium as compared with those taken a year ago and there is an increase in the calcium deposits in the epiphyseal lines in several places.

The best clinical estimate we can make in this case is one in which there is mild hyperactivity of the thyroid gland combined with disturbed function of the parathyroids. The report I believe serves to illustrate how the laboratory may aid the clinician in some of the difficult problems. Of course, cases such as this are rare

but the importance of help to the individual is great.

I have made the attempt in the foregoing remarks to present my ideas concerning the relative values of certain laboratory aids, in the domain of metabolism, in the study and management of the thyrotoxicoses. The impression I wish to leave with you is that while basal metabolism estimation, nitrogen studies and mineral balances may be of the greatest service, these aids are only safe if correlated with the general situation and their significance interpreted in the light of sound clinical judgment.

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# The Delayed Type of Allergic Reaction\*

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I THOUGHT it might be interesting to present, together with some illustrative cases, a type of hypersensitive reaction in man that has been little appreciated and is not well understood. The usual clinical conditions of asthma and hay fever are, generally speaking, immediate reactions, that is, the attack is precipitated very quickly within from one to thirty minutes after contact with the substance to which sensitiveness exists. In these cases the diagnostic skin test with this substance is also immediately positive, giving the typical urticarial wheal. It is in this group with the immediate clinical + test reactions that the sensitizing bodies are demonstrable by transfer of sensitiveness to normal human skin by means of the serum of a sensitive case. In this group also there is a great tendency to multiple reactions, that is, many clinical types of reaction, as well as reaction to many different substances. Here also we see a large group with positive antecedent family histories.

In contrast to this group, I want to call your attention to one that, for some reasons to be given later, seems properly to be classed as an allergic reaction. It, on the contrary, is char-

acterized by the delay in the onset of the clinical reaction and by the absence of any cutaneous test. It appears chiefly in cases in which histories of antecedent allergy are not obtained and the reactions are usually single. At the present time the diagnosis is entirely a clinical one. I have selected four typical cases to illustrate the type of reaction to which reference is being made.

The first case was one of a woman, age 31, whose family history was entirely negative for all forms of allergy, and whose past history was negative for any other type of allergic reaction. This woman comes from North Carolina. In the fall, at the time when it is the custom to indulge rather largely in pork, she had for a period of several months eaten rather excessively of pork. At the end of two months she began to have a generalized edema. This stopped within a few weeks after the ingestion of pork was stopped. At the end of several more weeks, not being thoroughly satisfied, she began again to use pork in smaller amounts, and the same reaction occurred, this time much more severe, so that there was a tremendous edema of the entire face, the eyes were tightly closed, and there was some edema of the larynx which obstructed breathing.

Two weeks later she had a similar attack after eating a small portion of

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\*Presented at the Boston Meeting of the American College of Physicians, April 10, 1929.

ham In this case, following continued use, there was a definite increase in the sensitiveness of the individual to pork In addition to the superficial angioneurotic edema, she had attacks of severe headache and abdominal pain that were probably of the same nature There was, however, no manifestation of any asthmatic attack Although in these cases treatment is not advisable, it was decided at least to determine by means of the intradermal test whether there was a sensitization or not, so that the test was made with the preparation of pork protein The actual amount given is very, very small There was no reaction at the site of the injection Six hours later, however, there suddenly developed nausea, backache, abdominal pain, general prostration, a generalized pruritus, and urticaria with angioneurotic edema which passed off entirely in twelve hours

A repetition of this test was done at the urgent request of the patient with identical results

Another case was that of a school teacher, age 32, who had no previous sensitizations When first seen she had a generalized urticaria which had been going on for a period of six months A careful history of her habits and diet developed the fact that nearly at the time of the onset of this trouble chocolate had begun to be used in rather unusual amounts, at least unusual for her The cutaneous reaction to a preparation of chocolate was done and it was entirely negative It was two weeks after she stopped eating chocolate that the urticarial eruption entirely disappeared Then following certain clinical observations, it was al-

ways possible after an incubation period of twenty-four or twenty-six hours to have a recurrence of urticarial lesions following the ingestion of the usual amount of chocolate However, she could always take a reasonable amount, a quarter of an eighth of this, for an indefinite number of days without developing any reaction whatsoever In other words, there is in this case, not only one of the typical delayed clinical reactions with absence of cutaneous reaction but a limit of toleration, a threshold beyond which she could not go without inducing symptoms

A third case is that of a woman about 35 years of age There was no antecedent history in her case and there was no personal history of allergy save for this particular thing One night after she had eaten some soft clams and in two or three hours suddenly became nauseated and faint Within a few hours there was a general urticaria and marked angioneurotic edema with headache and abdominal pain, but no vomiting and no diarrhea Other individuals who had had the same meal and who had eaten the same thing had no symptoms whatsoever In other words, it was not a type of ptomaine poisoning

Two weeks before the patient was seen she had again eaten some soft clams for the first time in four years In three hours there was a general urticaria, and this time no fainting occurred, but headache and abdominal pain were present as at first The intradermal tests were done, with an extract of the soft clam There was no immediate reaction to the test, but in the course of the six-hour period

there was considerable edema of the arm with itching and the development of a mild, general urticaria which passed off in fifteen hours

A repetition of this test gave the same period of incubation, that is a delay in the reaction of at least six hours and a mild general reaction following, which lasted for a period at this time of six to eight hours

The last case which I want to cite to illustrate this type of delayed allergy is that of a woman 31 years of age, who all her life had had a distinct sensitiveness for milk and eggs. They always produced a sense of nausea. They were taken, however, in small amount in cooked foods and in disguised form. Following the birth of her first child she was induced to take milk in amounts. Shortly after this began urticarial attacks which lasted until the diet was altered. On account, then, of the difficulty that she had in maintaining the proper nutrition, having become so extremely sensitive to milk, it was attempted to try to modify this by means of ingestion injection. Her sensitiveness, had developed to such a point that the equivalent of 0001 of a cubic centimeter of uncooked milk by subcutaneous injection would be followed by symptoms of urticaria and angio-neurotic edema, and before the attack passed off, a short attack of asthma. This happened not on one occasion but on a number of occasions. In this case, the cutaneous tests with the milk were themselves absolutely negative, and the reaction time from the injection to the development of urticaria was from five to six hours.

In all of these four cases the sensitization has occurred—mind you,

these are purely the striking cases that have been selected—to ordinary articles of diet, and reactions have followed the ingestion of quantities which, of course, would not produce any reaction at all in normal persons. It seems, then, perfectly justifiable to include these cases as a type of allergic reaction. The reactions also occur not only to foods but to drugs.

In these four cases there are several interesting features. In two of them the reactions have followed the use of these certain articles of foods over long periods of time, but in the other two cases, there has been no excessive use and the frequency of their administration has been minimal.

The other interesting point is the increase in the sensitiveness that has occurred, and in spite of this increase of sensitiveness there has been no appreciable shortening of the period of incubation, that is the period between the contact and the resulting symptoms. It seems proper to classify these cases as allergic on account of the typical clinical evidences of allergy reaction to common foodstuffs when taken in reasonable amounts. It may well be that a number of the cases that belong or are supposed to belong in the general group of allergic conditions are examples of the delayed reaction. Although there has been no proof as yet of the fact, it is the clinical experience of pediatricians that in certain cases of periodic vomiting definite improvement has been shown following the exclusion or the decrease in certain types of food in the diet.

As to the nature of the mechanism of this particular reaction, it is not known. One might be led to believe

that there was some analogy between it and serum disease. However, this analogy is not complete for the reason that although there is a delayed incubation period in serum disease at first, after serum disease, cutaneous reactions are possible and skin transfer of sensitiveness is also possible. So that we cannot at the present time assume that it is a form of induced sensitiveness analogous to serum disease.

As to the method that has to be pursued in the diagnosis of any case of this kind, of course it is obvious that in certain cases, as those cited, the reactions were either so intense or followed such an unusual type of food that the patient himself had made the diagnosis. But it is by no means necessary to stretch the imagination to suppose that many of our undiagnosed cases of allergic conditions belong in this same class and are not to be diagnosed by means of the immediate cutaneous reaction. The only resort that we can have at the present time is rather laborious and uncertain, one of variations in diet, the clinical method of trial and error.

My reason for presenting this paper is not only to bring forward an idea with regard to an unusual type of hypersensitiveness but to try to emphasize the difficulties that are inherent in this work. There are all sorts of combinations that may occur between

the clinical reactions and the cutaneous tests. In those cases of immediate clinical reactions, we usually get an immediate positive cutaneous reaction, but there are immediate clinical reactions like asthma and hay fever in which the cutaneous tests may be entirely negative. Here, however, we can assume, and very properly, a localization of the hypersensitive area. In the cases where there is a delay in the clinical reaction, immediate cutaneous tests could not be expected to occur. There are also instances in which, without any clinical manifestations at all, positive cutaneous reactions occur.

It seemed to me that this was perhaps an excellent opportunity to emphasize not only the use but the difficulties with, and the abuse of the skin test in diagnosis of allergic conditions. I want particularly to call attention to the fact that skin testing is only one procedure in the diagnosis of hypersensitive conditions. It is by no means a hundred per cent fool-proof. The importance of a clinical study in allergy is just as great as are the tests themselves which must be used only as an aid, and a good deal of common sense must always be employed in their interpretation. They cannot be accepted on their face value. It is always wise to make a careful clinical study and use tests merely as a guide.

# Serum Inorganic Sulphates In Addison's Disease

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IT HAS been shown<sup>2,3,5,6,7</sup> that during the critical periods and terminal stages of Addison's disease renal insufficiency may be manifested and is evidenced by the retention of urea and by inability of the kidney to excrete water and phenolsulphonephthalein. The amount of total solids in the urine also may be lessened.

The object of my study was to determine if the concentration of serum inorganic sulphates is increased in Addison's disease. Also, if serum inorganic sulphates were found to be increased I hoped to establish whether the increase is a constant feature of the disease or whether it occurs only during the critical periods and in the terminal stages, or, if retention of serum inorganic sulphates occurs only during the critical periods and terminal stages of the disease, then I hoped to establish the relationship of retention of sulphates to renal insufficiency.

Patients who came to The Mayo Clinic and who were hospitalized for treatment of Addison's disease were studied. During their stay in the hospital, determinations of serum inorganic sulphates were made in duplicate on two days in all but two cases.

\*Work done in the Division of Medicine under the direction of Dr L. G. Rowntree. Submitted for publication July 31, 1929.

The results are given in table 1. The sulphates were determined colorimetrically. As nearly as was possible, the conditions were kept constant. The diets were as constant as is possible in Addison's disease, for the diet is necessarily controlled by the capricious appetite of the patient.

In cases 4, 8, 11, 14, and 15 (table 1) there was an increase in serum inorganic sulphates. In case 8, blood for determination of sulphates was obtained on the day of death. In cases 3 and 5, the values (0.5 to 1.5 mg in each 100 c.c.) are higher than normal values for serum sulphate but are no higher than those frequently seen in patients in hospitals (from 2 to 3.5 mg in each 100 c.c.). In case 13 the value for urea was 49 mg in each 100 c.c. and the value for creatinine 3.5 mg in each 100 c.c. By more detailed analysis of cases 11 and 12, certain conditions will be identified which result in definite increases in serum inorganic sulphates.

In case 11, serum sulphates were definitely increased on the first determination. The patient manifested evidence of renal insufficiency. The concentration of urea in each 100 c.c. of whole blood was 106 mg and of creatinine, 2.4 mg. Excretion of phenolsulphonephthalein was estimated as 35 per cent in two hours. After the

TABLE I  
SERUM INORGANIC SULPHATES IN FOURTEEN CASES OF ADDISON'S DISEASE

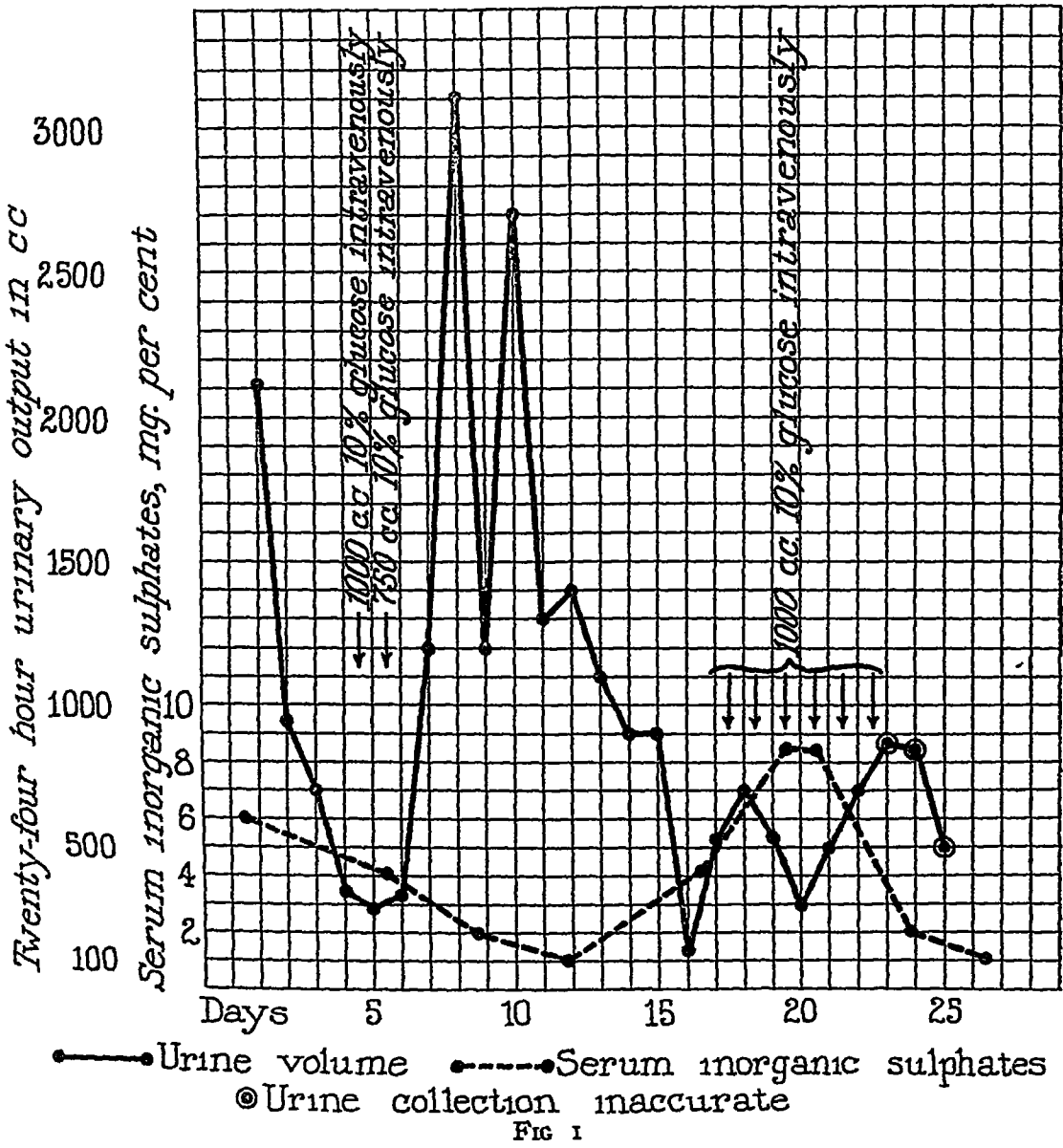
Cases	First determination	Second determination
1	0.9	1.3
2	2.0	2.1
3	2.8	3.4
4	3.5	4.6
5	2.6	3.0
6	1.5	1.9
7	0.7	
8	4.1	
9	3.1	3.6
10	3.0	3.0
11	7.2	4.2
12*		
13	7.8	6.0
14	3.0	2.8
15	3.5	3.6

\*Results are charted in figure 1

patient had been in the hospital for about one week and had received fluids intravenously, as well as all that he could take comfortably by mouth, the concentration of urea in the whole blood dropped to 42 mg and of the sulphates in the serum to 4.2 mg in each 100 c.c.

The patient represented in case 12 remained under observation for thirty-two days. He was very ill and had frequent gastro-intestinal upsets, with periods during which there was a decrease in the urinary output. The relation of serum sulphates to the urinary output is shown in figure 1. In this case the concentration of blood urea was normal (20 mg in each 100 c.c.). Excretion of phenolsulphonephthalein was 40 per cent in two hours. In figure 1 it is seen that the first determination of serum sulphate was made at the end of a period of four days during which less than 1 liter of urine was excreted daily. During this period the patient was very

ill, he was nauseated and frequently vomited, that is, he had just gone through one of the gastro-intestinal upsets which are common in the course of Addison's disease. Synchronously with the cessation of vomiting, the output of urine rose rapidly, and there was general improvement in his condition. The volume of the urine perhaps was increased by the 2 liters of solution of glucose given on the two preceding days. In the next interval of five days, the daily output of urine remained well within normal limits. The concentration of serum sulphates gradually returned to normal. Then there was a relapse, the nausea and vomiting returned, the output of urine decreased and the concentration of serum sulphates rose. In the first part of this relapse, the patient had a reaction following the intravenous administration of solutions of glucose, so that for a few days thereafter none was given. On the twentieth day after admission, the administration of so-



lution of glucose again was started and 1 liter of a 10 per cent solution was given daily for about six days. The concentration of serum sulphates fell rather rapidly to normal. The patient was very ill, he became psychotic and it was difficult to get him to take fluids by mouth, although he was not nauseated and did not vomit. Likewise, it was impossible accurately to collect the urine.

COMMENT

Previously, in a study of the effect of diuresis on the concentration of serum inorganic sulphates, it was found that the diuresis from the administration of salyrgan caused a slight but definite decrease in levels of serum sulphate. Patients with edema of renal origin were studied. A further observation made at that time was that during the water and concentra-

tion tests of Volhard and Fahr, the only significant changes in the concentrations of serum sulphates were observed in cases in which there was definite gross renal insufficiency. Increases in the serum sulphates were found during the concentration test and decreases after the water diuresis. That is, fluctuations in concentrations of serum sulphates can be made to occur by controlling the urinary output, especially if there is impaired renal function. The rise in the concentration of serum sulphates in case 12, in this study, is comparable to that in a prolonged concentration test, the patient was unable to take the fluid instead of it being withheld.

The renal insufficiency in Addison's disease is not manifested except during the critical periods and the terminal stages of the disease. This fact probably is significant, for it is at these times that the asthenia is the most marked. Definitely to correlate the renal insufficiency with the vascular asthenia would be difficult, if not impossible, and was not attempted in this study. The difficulty of making such a correlation is appreciated when one recalls that the blood pressure already is so low in the typical case of Addison's disease that the margin left for it to fall and still be compatible with life is very small.

The critical periods of Addison's disease are accompanied usually by nausea and vomiting. Often the vomiting is severe enough to cause not only lowered daily urinary excretion but mild dehydration. The question then arises as to whether the increased concentration of sulphates and urea is not a condition comparable to that

often seen in high intestinal obstruction. These two conditions are not the same, for the blood chlorides and the carbon dioxide combining power remain practically unchanged during the periods of vomiting in Addison's disease, whereas, in upper intestinal obstruction, altered values for the carbon dioxide combining power and chlorides may take place before any definite changes take place in the concentrations of the blood urea. From this evidence, it seems that renal insufficiency, probably from circulatory asthenia, is the important factor in the production of increased values for serum sulphates, and that if it were not for this renal insufficiency the amount of dehydration could hardly cause the increase in sulphates and urea so often seen.

Some experimental work on animals is cited which will help to establish the fact that impaired or suspended suprarenal function, with the subsequent circulatory asthenia, produces lowered renal function. In 1916, Marshall and Davis showed that when suprarenalectomized cats die, the urea content of the blood and tissues is much higher than that of normal animals. These experimenters made further studies, and found that after complete removal of the suprarenal glands, renal function was decreased in the interval before exhaustion and low blood pressure set in. Marshall and Davis did not determine the concentrations of the blood sulphates. In 1928, Swingle and Werner studied the chemistry of the blood after extirpation of the suprarenal glands in dogs and found that the inorganic sul-



phates may be greatly increased after such a procedure

#### SUMMARY

Concentrations of serum inorganic sulphates are normal in cases of

Addison's disease except during the critical periods and the terminal stages of the disease. The increase in the concentration of serum sulphates during these periods is an expression of renal insufficiency.

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# Phosphorus In The Blood And Urine: A Study Of The Excretion And Retention Of Phosphorus In A Normal Subject And In Patients With Renal Disease\*

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THE rôle of inorganic chemical compounds in the physiologic processes of man remains elusive. This paper is the report of studies on the significance of inorganic compounds of phosphorus as related, especially, to the urinary excretion in the normal person and in patients with renal injury. The effect of oral and intravenous administration of phosphatic compounds on the level of phosphorus in the blood and on the amount of urinary phosphorus excreted is studied in normal subjects and in patients with nephritis. An understanding of how frequently phosphorus is involved in almost all physiologic processes can be gathered from the very complete review by Forbes and Keith of all literature dealing with phosphorus as related to animal life. Bergmann showed that sodium phosphate

injected subcutaneously into dogs appeared entirely in the urine and that the path of excretion was not altered even though the intestine was laden with calcium. He found, though, that in sheep the injected phosphorus appeared almost entirely in the feces.

Elias and Weiss injected solutions of phosphate intravenously in patients with diabetes and in normal control subjects in an investigation on the effect of phosphates on blood sugar. As far as I know, these are the only investigators who, up to the time of my work, have introduced solutions of phosphate directly into the blood stream of man. The effect of intravenous injection of solutions of phosphate has been studied mainly in animals, chiefly in dogs and rabbits. Binger, Salvesen, Hastings and McIntosh, and Tisdall were able to obtain a decrease in the level of calcium and an increase in the level of phosphorus on injection of solutions of sodium phosphate. They obtained tetany when using alkaline or neutral solutions. Lehman injected into rabbits for each kilogram of body weight from 50 to 75 mg of phosphorus in the form of acid sodium phosphate. An immediate rise of the inorganic phosphorus in

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\*Abstract of thesis submitted to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Medicine, March, 1928. This work was done in 1927 and 1928. Since then, similar work, but with organic phosphates, has been done by R. T. Bain and H. D. Kay, working in Arthur Ellis' Clinic at the London Hospital. Submitted for publication July 3, 1929.

the blood occurred and this was followed by a return to normal within four hours. He obtained tetany in some cases in spite of the fact that he used the acid salt. Addis, Meyers, and Bayer noted an immediate rise of the amount of phosphorus in the plasma and urine, with a gradual fall to normal or below. They used a solution of the acid and alkaline salts adjusted to a hydrogen-ion concentration of 7.4 and injected into rabbits an amount equivalent to 25 to 50 mg of phosphorus for each kilogram of body weight. In 1872 Falck injected into dogs from 0.6 to 1.3 gm of sodium phosphate for each kilogram of body weight. He obtained a peak in urinary phosphorus in between one and two hours after injection, and this was followed by a gradual fall, which reached normal in from six to nine hours after injection. Frey's experiments showed a continuing rise in the output of urinary phosphorus at three hours after injection, although the level of phosphorus in the serum had fallen remarkably by that time. Underhill injected neutral sodium phosphate into cats and found the greatest change in the plasma. He also noted that the rate of disappearance from the plasma is much slower for phosphorus than for either urea or creatinine. Iversen showed an immediate rise and a rapid fall of the level in the plasma after injection of phosphorus, but in the cells the level rose slowly and continued to rise when the level in the plasma was falling.

The significance of phosphorus in nephritis can well be measured by the large number of articles on this subject. Fleischer noted diminished ex-

cretion of phosphorus in nephritis with a change in the content of phosphorus of the feces. Kovesi and Roth-Schultz, as recorded by von Noorden, found almost constant retention of phosphorus in cases of nephritis, this was especially marked in cases in which edema was developing. The relation levels in the blood of inorganic phosphorus and of nonprotein nitrogen in nephritis were studied by Greenwald. He found that they usually ran parallel, but in isolated cases he obtained a high value for serum phosphorus with a low value for nonprotein nitrogen, or just the reverse. Denis and Minot noted a striking pre-mortem rise in plasma phosphorus in all fatal cases of nephritis. In two nonfatal cases there was not a rise to alarming heights. They found no constant relation between retention of phosphorus and the amount of nonprotein nitrogen. In fact, in several of the fatal cases there was normal nonprotein nitrogen, whereas in cases in which the patients recovered the nonprotein nitrogen was high and the blood phosphorus and phenolsulphonephthalein return were normal. Twenty-two cases of nephritis and cardio-renal disease were reported by Denis and Hobson. Of these, there was increase of inorganic phosphorus in the blood in 45 per cent. Salvesen and Linder studied fifteen cases of Bright's disease. Uremia occurred in two of these and was associated with severe retention of phosphorus.

The significance of retention of phosphorus as a prognostic sign was noted by Schmitz, Rohdenburg and Myers. However, they found that the amount of creatinine ran parallel to

the retention of phosphorus and that the latter was as reliable a sign, if not more reliable, than the former. Their results disclosed a rather constant low level of calcium in the blood in patients with retention of phosphorus. DeWesselow reported eight cases in which the patients died with symptoms of uremia. In all of these there was severe retention of phosphorus, although the blood urea was not markedly elevated in all cases. On the strength of this observation, DeWesselow also considered that severe retention of phosphorus offered a grave prognosis. He noted that the levels of calcium were below normal in a high percentage of cases and suggested that the administration of calcium salts might have some therapeutic value. Marriott and Howland believed phosphorus to be the cause of acidosis in nephritis. They also advised administration of calcium as a means of eliminating phosphorus. This suggestion was based on the rather great frequency with which a low amount of calcium was found with retention of phosphorus and also on the observation that the ingestion of large amounts of calcium caused increased excretion of phosphorus in the feces. However, Bergmann previously had shown that in carnivora all the phosphorus in the stool comes from the phosphorus ingested and that calcium does not draw any phosphorus from the blood into the intestine. In this connection it might be well to mention the work of Boyd. She administered calcium chloride and calcium lactate to children with nephritis and brought about an improvement of edema. However, the calcium did not affect

the blood phosphorus or the acidosis as suggested by Marriott and Howland. Halverson, Mohler, and Bergheim could find no effect of the administration of calcium in cases of uremia and severe nephritis, even though there was an associated low blood calcium. Fetter noted great retention of inorganic phosphorus in nephritis with acidosis and suggested that the phosphorus is retained to maintain the physiologic reaction of the blood. He believed that the retained phosphorus causes phosphorus acidosis and, in contrast to Marriott and Howland, suggested that this can be relieved by the administration of more phosphorus. One case is reported and in this he obtained favorable results with the treatment. Boyd, Courtney, and MacLachlan reported the results of two years' study on thirty-three cases of nephritis. Increase of plasma phosphorus was found in 66 per cent of cases and decrease of calcium occurred in 71 per cent. The inverse ratio of phosphorus to calcium was present only in cases in which the levels were far from normal.

#### METHOD OF EXPERIMENTS WITH TABULAR AND GRAPHIC REPRESENTATION OF RESULTS

The work here recorded may be divided into four studies. In the first, the output of phosphorus\* in the ur-

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\*It should be noted that the determinations for phosphorus in the blood and urine were for inorganic phosphorus, and those for phosphorus in the feces were for total phosphorus. To avoid monotony in the paper, the unmodified term "phosphorus" has been used in many instances in which the concern has been with total phosphorus or with inorganic phosphorus.

me, as described by Haldane, Wigglesworth, and Woodrow, was studied in a normal subject and in two patients with renal injury (tables 1, 2 and 3) This curve was followed only during the morning hours After the previous evening meal, the subjects were not allowed to have food Water

was given in moderate amounts. Breakfast was withheld and a known amount of water, usually 500 cc, was given at 8 00 a m Urine was collected hourly after 7 00 a m and until 12 00 noon All specimens were measured and preserved with chloroform, whether they were examined

TABLE 1—NORMAL OUTPUT OF PHOSPHORUS IN A HEALTHY SUBJECT UNDER CONTROLLED CONDITIONS\*

Hour	Urine				Blood		Plasma
	Volume, c c	Phosphorus, mg		H <sub>p</sub>	Inorganic phosphorus, mg in each 100 c c	Serum calcium, mg in each 100 c c	Carbon dioxide, combining power, per cent by volume
		In each c c	Each hour		Whole blood		
11 p m to							
7 a m	240	1 07	32 1	5 7			
8 a m	35	0 59	20 8	5 5	3 27	3 37	10 0
9 a m	65	0 17	11 2	5 4			67
10 a m	310	0 03	10 1	5 8	3 15	3 02	9 6
11 a m	68	0 17	12 0	5 5			59
12 noon					3 02	2 89	10 3
12 20 p m	50	0 33	12 6	5 5			59

\*The subject did not have breakfast but drank 500 cc of water at 8 a m

TABLE 2—OUTPUT OF PHOSPHORUS UNDER CONTROLLED CONDITIONS,\* IN A CASE (CASE 1) OF CHRONIC GLOMERULONEPHRITIS WITH UREMIA

Hour, a m	Urine				Blood		
	Phosphorus, mg				Inorganic phosphorus, mg in each 100 cc		Serum calcium, mg in each 100 cc
	Volume, cc	In each cc	Each hour	H <sub>p</sub>	Whole blood	Plasma	
5 to 7 30	290	0 17	19 7	4 8	7.73	7 88	67
9 00	210	0 17	24 9	5 8			
10 30	170	0 18	20 7	5 4			
12 noon	190	0 16	21 3	5 6			

\*The patient did not have food for fourteen hours but drank 250 cc of water every hour

TABLE 3—OUTPUT OF PHOSPHORUS UNDER CONTROLLED CONDITIONS,\* IN A CASE (CASE 2) OF MALIGNANT HYPERTENSION WITH UREMIA

Hour	Volume, cc	Urine Inorganic phosphorus, mg		pH	Blood	
		In each cc	Each hour		Inorganic phosphorus in plasma, mg in each 100 cc	Serum calcium, mg in each 100 cc
4 to 7:30 a m	60	0.25	3.8	6.6	7.4	8.9
9 00 a m	60	0.26	10.5	7.2	7.8	
10 30 a m	60	0.26	9.1	6.0		
12 noon	75	0.27	13.1	5.6	7.6	
1 30 p m	80	0.27	14.5	5.4		
3 00 p m	60	0.29	11.7	6.6		
4 30 p m	80	0.28	15.3	5.6		

\*The patient did not have breakfast or lunch but drank 250 cc of water every hour

immediately or not. The inorganic phosphorus, and in some cases the hydrogen-ion concentration, of each specimen was determined. For the latter, Gillespie's method, as described by Clark, was used. The hydrogen-ion concentration was studied to see whether any variation of the curves of phosphorus and of alkali occurred in cases of renal injury. In several cases the levels of inorganic phosphorus in whole blood and plasma were obtained to determine whether or not these changed with the curve of output. The blood urea, creatinine, serum calcium, inorganic phosphorus, and return of phenolsulphonephthalein were determined in every case of injury. This curve of the output of phosphorus obtained under the same controls as described here, was determined later in all cases in which sodium phosphate was administered. Thus, the curve of the output of phosphorus was determined for each subject, whether healthy or diseased. The name "control day" will be applied to this day on

which the curve that was "normal" for each person was determined.

In the second series of studies, the effect was noted of oral administration of acid and alkaline sodium phosphate on levels of inorganic phosphorus in blood and urine. Two persons were studied, one a healthy subject (table 4) and the other a patient with chronic glomerulonephritis and subsiding uremia (table 5). A control day, preceding the day of administration of sodium phosphate was obtained for each subject. The same conditions were maintained on the day of administration. To the normal subject, 7 gm of acid sodium phosphate, and to the nephritic patient, 12 gm of the alkaline salt were administered early in the morning. The serum calcium and the inorganic phosphorus of the whole blood and of the plasma were determined before ingestion of the salt and at intervals thereafter. The urine was collected at hourly intervals and analyzed for inorganic phosphorus. The results

TABLE 4—VALUES FOR PHOSPHORUS UNDER CONTROLLED CONDITIONS\* IN A HEALTHY SUBJECT, OUTPUT OF PHOSPHORUS AND LEVELS IN THE BLOOD

Date, December	Hour	Urine			Blood			Comment
		Volume, cc	Phosphorus, mg		Inorganic phosphorus, mg in each 100 cc		Serum calcium, mg in each 100 cc	
			In each cc	Each hour	Whole blood	Plasma		
27	8 30 a m	33	0.95	31.4	3.32	3.33		Control day
	9 30 a m	240	0.07	18.6				
	10 30 a m	750	0.02	15.7				
	11 30 a m	600	0.02	15.1				
	12 30 p m	160	0.12	20.4				
28	8 30 a m	30	0.64	19.4	4.25	3.70	10.8	7 gm of acid sodium phosphate administered orally at 8 45 a m
	9 15 a m	37	0.51	25.0	4.90	5.00	10.8	
	10 15 a m	190	0.35	66.2	4.65		9.6	
	11 15 a m	510	0.14	72.8				
	12 15 p m	510	0.13	66.6	4.54	4.30	10.0	

\*The subject did not have food for the preceding fourteen hours but drank 250 cc of water every hour

TABLE 5—VALUES FOR PHOSPHORUS UNDER CONTROLLED CONDITIONS\* IN A CASE (CASE 3) OF CHRONIC GLOMERULONEPHRITIS AND SUBSIDING UREMIA

Date, December	Hour, a m	Urine				Blood		Comment
		Volume, cc	Phosphorus, mg			Inorganic phosphorus, mg in each 100 cc	Serum calcium, mg in each 100 cc	
			In each cc	Each hour	pH	Whole blood	Plasma	
15	7 30	200	0.27	10.8	5.6	4.4	4.4	Control day
	9 00	45	0.33	9.9	5.2			
	10 30	90	0.32	19.2	5.4			
	12 noon	90	0.36	21.6	5.4			
16	7 30	260	0.32	16.6	5.6	4.8	4.7	12 gm of alkaline sodium phosphate administered orally at 8 00 a m
	9 00	80	0.46	24.4	5.2			
	10 00	80	0.48	40.4	5.0	5.1	5.5	
	11 00	70	0.47	32.9	5.0			
	12 noon	110	0.37	40.7	5.8	4.7	5.1	

\*The patient did not have food for fourteen hours but drank 500 cc of water at 7 a m

were charted and compared with those obtained on the control day. Later, 1.4 gm of the salt was administered to the healthy subject (table 6). Urine was not obtainable because of the laxative effect. However, the levels of phosphorus in the blood were determined and charted.

TABLE 6—THE LEVELS IN THE BLOOD OF INORGANIC PHOSPHORUS AND OF CALCIUM IN A HEALTHY SUBJECT

Hour, a m	Phosphorus, mg in each 100 c c		Serum calcium, mg in each 100 c c	Plasma Carbon dioxide capacity, per cent by volume
	Whole blood	Plasma		
* 8 30	3.62	3.10	10.6	67
9 30	4.52	5.03		57
10 30	4.26	4.83	11.0	61
11 30	4.11	4.39	10.6	56

\*Ingestion of 1.4 gm acid sodium phosphate

Up to this point, the amount of inorganic phosphorus of the blood and of the urine was determined by the Briggs modification of Bell-Doisy's method. This method was not the most satisfactory, for the colorimetric solution faded too rapidly and only a small number of determinations could be made with each standard. For later studies, the method of Fiske and Sudbarrow was used. This proved to be accurate and allowed for more determinations to be run simultaneously because of the stable color of the solutions. With both methods, determinations of blood were run through immediately for it has been found (Zucker and Gutman and others) that the inorganic phosphorus undergoes

changes when allowed to stand in whole blood, producing a higher level of phosphorus for whole blood and a lower level for plasma than really is present in vivo. The blood was centrifugalized immediately, hematocrit readings were taken, and the plasma was drawn off. Throughout, only the inorganic phosphorus was determined, except in the feces, in which determinations of the total phosphorus were made. The method for the determination of serum calcium also was changed. Earlier, the Tisdall modification of the Kramer-Tisdall method was used. For later studies, the Clark-Collip modification was used. Blood urea was determined with the Marshall method as modified by Van Slyke and Cullen. The method of Folin and Wu was used for the determination of blood creatinine. The level of uric acid in the blood was determined only a few times, the method described by Benedict was used. The carbon dioxide combining power of the plasma was determined by the volumetric method of Van Slyke and Stadie.

In the oral administration of sodium phosphate many factors are involved which interfere with the obtaining of consistent results. Chief of these are the rate and amount of absorption from the intestine and the laxative effect of the salt. This method of approach was discarded and an attempt was made to find a solution containing phosphorus which could be given intravenously with safety. A solution of sodium phosphate, here described, finally was developed and proved very satisfactory. A solution of acid sodium phosphate (9 per cent)



was added to a solution of alkaline sodium phosphate (96 per cent) in a ratio of three parts of the former to seventeen parts of the latter. By calculation and analysis, this contained 17.2 mg of phosphorus in each cubic centimeter. This solution gave a hydrogen-ion concentration of 7.1 to 7.2 after being autoclaved. It was prepared in amounts of 200 cc and was kept in stoppered flasks of pyrex glass. The solution never was kept more than four days. Massive doses were injected into a dog without any symptomatic effect. Seventy-three cubic centimeters (400 mg of phosphorus) was injected intravenously into a dog which weighed 11 kg (table 7). Catheterized specimens of urine were taken every fifteen minutes and samples of blood were taken before

injection and at intervals after injection. Three hours after the first injection, 55 cc (950 mg. of phosphorus) was given, also without noticeable effect. The blood and urine were examined for their content of inorganic phosphorus. Intradermal wheals of the solution of phosphate were not painful, so it was considered safe to attempt intravenous injection into a human subject. Starting with 5 cc at the first injection, the dose was increased daily until the maximal dose of 61 cc (1050 mg of phosphorus) was reached. In a man who weighed 70 kg this dose equalled 15 mg of phosphorus for each kilogram of body weight. Ten minutes were taken to complete the injection and subjective effects were not noticed at any time. This rather large dose was more than two times the size of any dose given after this time, and was used only to give assurance that smaller doses could be administered with safety. The effect of injection of the solution of phosphate on levels in the blood and urine was not determined until a dose of 118 mg of phosphorus for each kilogram of body weight was reached. The total for a man weighing 72.2 kg would be approximately 852 mg. This was done on a healthy adult male. The conditions on the day of injection were controlled in a manner similar to that in which they were controlled on a preceding control day. The solution was injected at 8:15 a. m. Urine was collected at hourly intervals and analyzed for inorganic phosphorus and to determine the hydrogen-ion concentration. Blood was drawn before injection and at intervals thereafter.

TABLE 7—CONCENTRATION OF INORGANIC PHOSPHORUS UNDER CONTROLLED CONDITIONS \*IN URINE AND BLOOD IN A DOG WEIGHING 11 KG

Hour a. m.	Urinary phosphorus, mg in each cc	Blood Phosphorus mg in each 100 cc		
		Whole blood	Plasma	Serum calcium mg in each 100 cc
*9:30	0.44	6.26	7.34	10.8
9:45	2.47			
9:50	3.62			
9:55	3.49			
10:00	3.09	12.2	12.4	
10:15	2.11			
10:30	2.15	10.3	11.3	9.2
10:45	2.43			
11:30	2.17	8.41	8.34	8.3

\*The dog did not have food for fifteen hours. Urine was collected by catheterization.

\*\*Injection of 23 cc (400 mg phosphorus) of solution of phosphate.

Determinations were made for serum calcium, plasma carbon dioxide combining power, and inorganic phosphorus of the whole blood (fig. 1)

In the third series of studies, this same subject was given a controlled weighed diet which contained a minimal and known amount of salts and he was allowed a fixed daily intake of fluid (table 8). The activity and meals were routine from day to day. The diet consisted of 2,500 calories, with 60 gm of protein, 126 gm of fat, and 266 gm of carbohydrate. The

total fluid in the food was 930 cc each day. In addition to this, 1,400 cc of fluid was taken in beverages and as water. The inorganic constituents of the diet in grams each day were as follows: sodium 0.72, potassium 2.83, magnesium 0.19, sulphur 0.71, iron 0.014, chlorine (as chlorides) 0.84, calcium 0.92, and phosphorus 0.93.

This diet was carried through for nine days. All feces and urine were collected and measured. The urine was collected at regular hours during

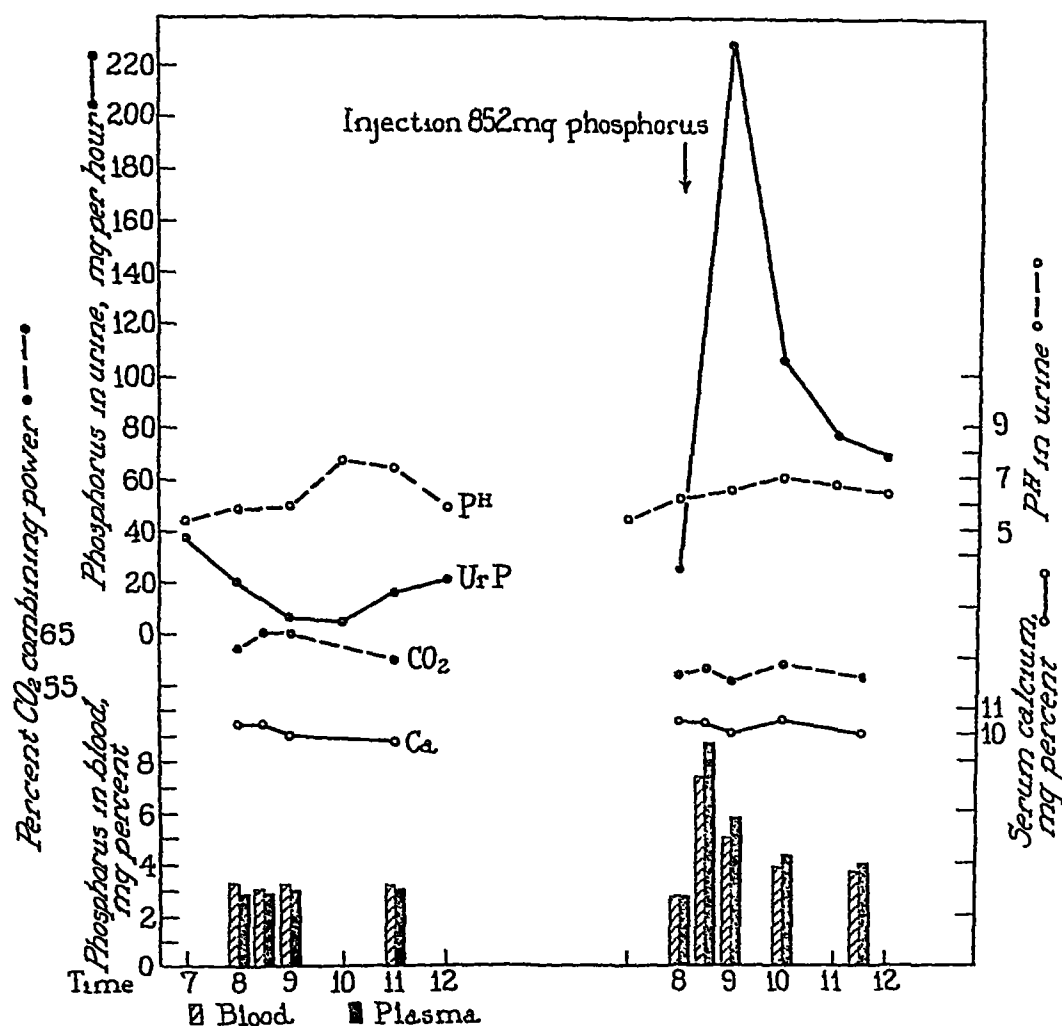


FIG. 1. The levels of constituents in urine and blood in a normal subject on a control day, and after injection of 852 mg of phosphorus.

TABLE 8—DAILY EXCRETION OF PHOSPHORUS AND CALCIUM IN 24 HR. URINE AND FECES OF A HEALTHY SUBJECT DURING A PERIOD OF CONTROLLED DIET

Date, December	Calcium, mg			Phosphorus, mg		Ratio of phos- phorus in feces to phosphorus in urine	Comment
	In urine	In feces	Total	In urine, inorganic	Feces, total		
3 to 4	55	660	715	86.4	328	1 : 2.6	
4 to 5	60	836	896	134.4	50.4	1 : 2.6	837 mg phosphorus injected
5 to 6	56	566	622	79.5	30.7	1 : 2.5	
6 to 7	57	227	284	6.46	13.2		Small amount of stool passed
7 to 8	62	543	605	146.8	49.5	1 : 2.9	875 mg phosphorus injected

the day, and during the morning it was collected every hour. Each specimen was analyzed for hydrogen-ion concentration and for content of inorganic phosphorus, and the twenty-four hour total was analyzed for calcium. Every specimen of stool was examined for calcium and for the total amount of phosphorus. Injections of the solution of sodium phosphate were made on the fourth and seventh days. On these days, and on the third day, samples of blood were taken at intervals during the morning and determinations were made for serum calcium, carbon dioxide combining power, and phosphorus of the whole blood and of the plasma. On the eighth and ninth days, calcium lactate was given orally. On the ninth day this was followed by injection of solution of phosphorus. Several weeks later the same subject was placed again on the same diet for six days (table 9). During this period, 5 gm of calcium chloride was given orally in solution on the second, third, and

fifth days. On the fifth day, this was followed by intravenous injection of solution of phosphate. On the second, third and fifth days samples of blood were taken at intervals during the morning, after ingestion of calcium. The specimens of urine and stool were collected and treated as they were treated during the preceding period of diet.

The method of analyzing the feces should be described. The stools were passed into weighed porcelain dishes, were dried over a steam bath, and the weight of the dried material was noted. This was allowed to cool and then was pulverized. Of this powdered material, 0.25 gm was accurately weighed out on a clean watch glass and washed into a hard glass nitrogen tube with from 3 to 4 cc of water. To this was added 2.5 cc of concentrated sulphuric acid. The tube, with its contents, was placed in a steam bath for from eight to twelve hours. This procedure breaks up the larger particles, and a thick black "so-

TABLE 9—DAILY EXCRETION OF PHOSPHORUS AND CALCIUM IN URINE AND FECES OF A HEALTHY SUBJECT DURING SECOND PERIOD OF DIET

Date January	Calcium, mg			Phosphorus, mg			Comment
	In urine	In feces	Total	In urine, inorganic	Feces, total	Ratio of amount in feces to amount in urine	
5 to 6		1251					4.4 gm calcium chloride orally
6 to 7	130	1002	1132	884	286	1.3	5.2 gm calcium chloride orally
7 to 8	60	407	467	945	121		
8 to 9	120	1941	2061	1814	762	1.24	5.2 gm calcium chloride orally, 1050 mg phosphorus in- travenously (unusu- ally large amount of feces excreted)

lution" is formed. After several glass beads had been placed in the tube to inhibit "bumping" it was held over a micro-burner and was allowed to heat slowly to a point at which the solution bubbled gently. Care was taken that it did not boil vigorously. After about fifteen minutes of this heating, concentrated nitric acid was added drop by drop until the solution was clear. Heating and the addition of nitric acid were continued until the solution was colorless and clear. This was then washed into a volumetric flask with a capacity of 50 cc and water was added to the mark. From 2 to 5 cc of this solution was then analyzed for phosphorus according to the method of Fiske and Subbarow. Molybdate solution II was used and was found to be more efficient than molybdate solution III. The amount of phosphorus found in 50 cc of solution equalled the amount in 0.25 gm of dried feces. The total amount

in the specimen could be calculated from this. The method of digestion here described was very satisfactory and proved to be accurate under several checks.

The fourth series of studies was performed on subjects suffering from renal disease. Figures 2, 3, and 4 are illustrative of these. This involved the injection of the phosphate solution intravenously. In view of the apparent nontoxicity, as found in the previous injections into a healthy subject, the solution was considered safe enough to administer to patients with renal injury and retention of phosphorus. The solution was administered to determine the rate and amount of phosphorus which could be excreted through the kidneys as compared with the output in a normal subject. Therefore, eleven subjects, ten patients with renal disease and one healthy subject were included in this series. An equivalent of 6.5 to 6.6

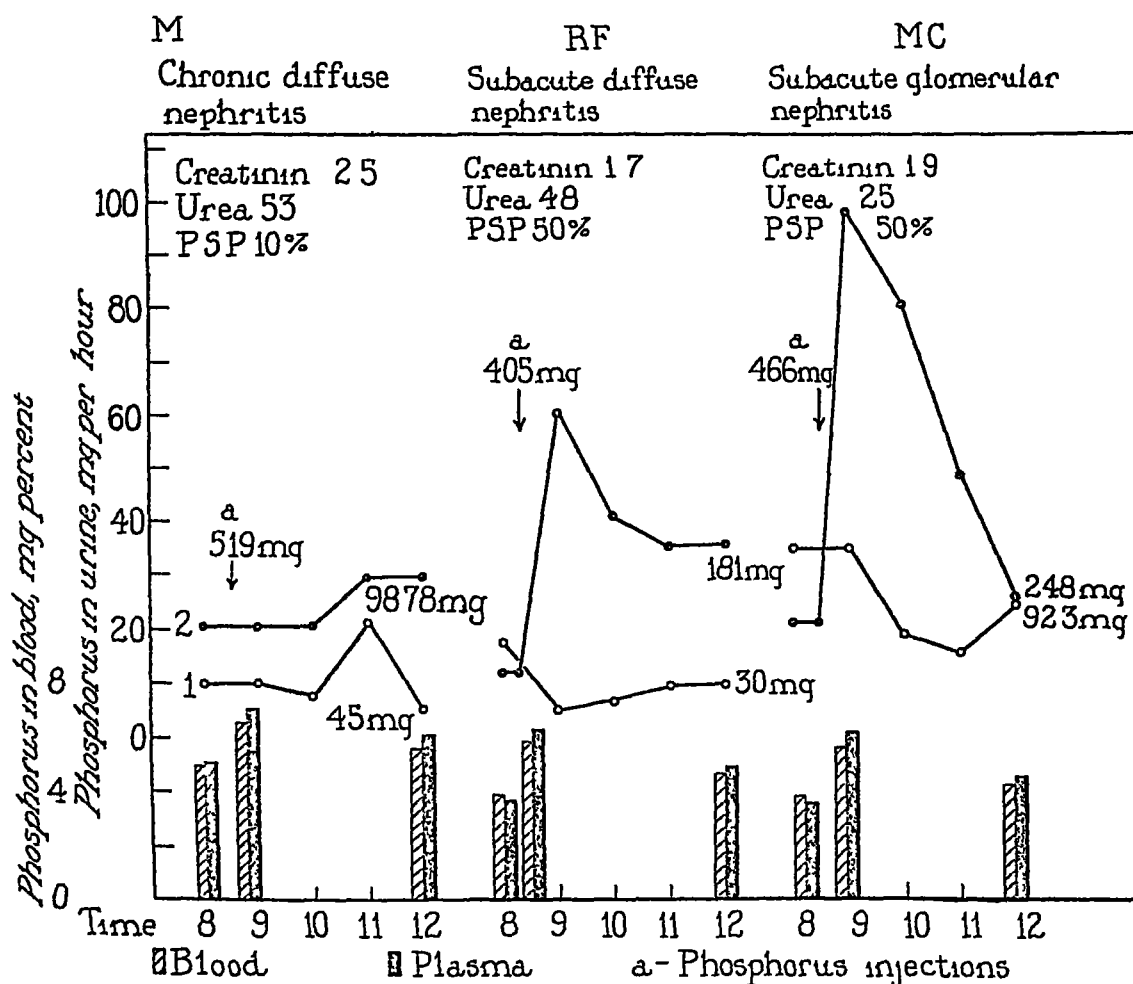


FIG 4 Values for phosphorus and other constituents in three patients with subacute and chronic nephritis (M, RF, and MC) in this figure and cases 11, 12 and 13 in table 10 (1) Output of phosphorus in urine on a control day (2) Output of phosphorus in urine and levels of phosphorus in blood before and after injection of solution of phosphate

phritis Many experiments have been described, and observations reported, to throw light on this subject The studies and results described in this paper are an attempt to add to the knowledge of metabolism of phosphorus in health and in renal disease

The normal level of inorganic phosphorus in the blood is from 2.5 to 4.0 mg in each 100 cc In a normal subject, the levels in the plasma and in the cells are probably the same As a rule, it is found that the level in the plasma is lower than that in the

whole blood It is known that, if whole blood is allowed to stand, the inorganic phosphorus diffuses into the cells Zucker and Gutman obtained a value for phosphorus in the cells two times that of the value for phosphorus in the plasma after they had allowed blood to stand five hours or more By the time the blood has been centrifugalized and the plasma drawn off, some diffusion already has occurred, thus a higher value for inorganic phosphorus in the whole blood would be obtained In my observation of the normal subject, the level of inorganic

phosphorus always was a trifle higher in the whole blood, even though determinations were made immediately

In cases of nephritis with retention of phosphorus this is not found true. The value for phosphorus in the plasma is consistently higher in these patients. In table 10 are found seven

cases in which retention of phosphorus in the plasma was more than 40 mg in each 100 cc. In case 2, determinations were not made on the whole blood. Only in case 3 was the level of phosphorus in the whole blood equal to that in the plasma. In cases 1, 8, 9, 10, and 11, the level of phos-

TABLE 10.—RESUMÉ OF RESULTS OF CHEMICAL EXAMINATION OF THE BLOOD IN THIRTEEN CASES OF RENAL INJURY. ALSO A COMPARISON OF THE RETURN OF INJECTED PHOSPHORUS WITH THE RETURN OF PHENOLSULPHONEPHTHALEIN

Case	Inorganic phosphorus mg in each 100 cc		Plasma		Whole Blood			
	Whole blood	Plasma	Carbon dioxide capacity, per cent by volume	Serum calcium, mg in each 100 cc	Creatinine, mg in each 100 cc	Urea, mg in each 100 cc	Return in urine of injected phosphorus, per cent	Return in urine of phenolsulphonephthalein, per cent
1	77	78	32	67	140	233		
2		77		89	98	238		10
3	44	44	34	86	38	85		30
4	34	31	50	102	19	43	59	80
5	35	34	54	108	19	42	55	75
6	32	32	53	112	50	87	10	10
7	39	38	57	104	37	62	25	25
8	60	63	38	97	87	182	9	5
9	53	55	47	76	19	49	22	20
10	42	43	47	93	30	50	17	10
11	50	50.9	51	87	25	53	10	10
12	39	38	46	93	17	48	37	50
13	37	35	63	106	19	25	33	50

phorus in the plasma during fasting was higher than that in the whole blood. The difference is more marked when the retention of phosphorus is greater. The same proportion was found in many other cases not recorded here. This would indicate that some abnormal mechanism, possibly the same as that which produces the retention, has a tendency to hold the phosphorus in the plasma.

The suggestion often has been made that the retention of phosphorus is

closely related to acidosis. Some have maintained that the retention is the cause of the acidosis, others have felt that the retention is the result of the acidosis. My results are not conclusive evidence that the two are related. In cases 1, 3, and 8 (table 10) the carbon dioxide combining power was below 40 volumes per cent. There were severe phosphorus retention and high blood urea in cases 1 and 8. In the other case (case 3), there was only mild retention of both phosphorus and

urea On the other hand, in cases 9, 10, and 11, in which also there was retention of phosphorus, there was no evidence of acidosis These cases, also, exemplified only slight retention of urea

The level of serum calcium seems to have a closer relationship to content of phosphorus than does the carbon dioxide combining power of the plasma In seven cases of retention of phosphorus, five (cases 1, 2, 3, 9, and 11) were associated with a value for serum calcium below 9.0 mg in each 100 cc In the one case (case 8) in which there was severe retention of phosphorus there was a calcium level of 9.7 mg in each 100 cc A value for serum calcium of 9.3 mg in each 100 cc was obtained in two cases, in one of which (case 12) the value for phosphorus in the serum was normal and in the other of which (case 10) there was retention of phosphorus Five patients with renal disease in whom the value for phosphorus was normal also had a serum calcium above 10.0 mg in each 100 cc Apparently Boyd was correct in her conclusion that the inverse proportion of calcium to phosphorus exists only when the levels are far from normal There occurred but one exception to this (case 8) in my series

Study of the levels of creatinine given in table II demonstrates that retention of phosphorus is frequently associated with a high concentration of creatinine in the blood Among eight patients (cases 1, 2, 3, 6, 7, 8, 10, and 11) with an elevated value for creatinine, there was retention of phosphorus in six These six died of nephritis within four months of the

time of examination One patient (case 6) who did not have the associated retention of phosphorus also died One patient (case 9) with retention of phosphorus had a normal value for creatinine This patient and the one (case 7) with a high value for creatinine, without retention of phosphorus, did not die In chronic nephritis it will be admitted that retention of creatinine and of phosphorus usually offers a fatal prognosis However, I agree with Schmitz that creatinine furnishes the more reliable sign

It has been stated often that retention of phosphorus is always associated with retention of urea Several investigators, however, have shown that patients may have severe uremic symptoms without real retention of urea In these cases they have found marked retention of phosphorus, and have attributed the symptoms entirely to the retained phosphorus Even though this is accepted as true, my results do not give evidence of such a conclusion Retention of urea occurred in all patients with an elevated value for creatinine Three cases with retention of urea, without an increase in inorganic phosphorus, are represented in table II (cases 6, 7, and 12). In two of these (cases 6 and 7) there was retention of creatinine Only case 6 was fatal and in that the value for creatinine was 5.0 mg in each 100 cc of blood

The concentration of phosphorus varies considerably in the urine if the renal function is normal In a normal subject, after injection of phosphorus, the concentration in each cubic centimeter of urine was 6.4 mg In cases

4, 5, 12, and 13 (table 10), the concentration was above 10 mg in each cubic centimeter. In nephritis of the glomerular type, with definite renal injury, there occurs a tendency to fixation of concentration of phosphorus, depending on the degree of injury. This is seen in tables 2, 3, and 4 where the concentrations are charted. In these and in cases 6, 7, 8, 10, and 11 in table 10 the urinary concentration of phosphorus never was higher than 0.5 mg in each cubic centimeter. In case 9, in which renal disease was definite, the concentration was 0.76 mg in each cubic centimeter. One would suspect that injury to the kidney, as in case 9, would alter the curve of the output of phosphorus as obtained in the normal subject by Hawk and Chamberlain and others. I obtained this curve in the normal subject, both when the subject was fasting and when he was receiving the diet low in salt, and also in patients with nephritis. The output of phosphorus in the normal person was independent of diuresis. A suggestion of the curve is seen in tables 2, 3, and 4, but the amount of phosphorus excreted each hour is wholly dependent on the amount of urine passed.

The cause of the type of curve of the output of phosphorus, as it occurs in the normal subject, has not been determined. The best explanation seems to be that based on the work of Marshall and Crane. They show that the variation in output of urinary constituents is dependent, to a greater or less degree, on the rate of flow of blood through the kidneys. This could account for the "alkaline tide"<sup>27,28</sup> and for the curve of the output of phos-

phorus. It is significant that the two occur at the same hours (table 1). It was suggested at one time that the change in the output of phosphorus was due to a change in reaction of the blood and urine. However, it has since been shown that the two are independent of each other. Ingestion of sodium bicarbonate increases the alkalinity of the blood and urine without perceptible change in the levels of phosphorus in either blood or urine. It is also found that intravenous administration of the solution of phosphate increases levels of phosphorus in urine and blood without change in the alkaline tide. The carbon dioxide capacity of the plasma also shows little change after the injection of phosphorus.

A picture of the path of excretion of phosphorus and calcium can be obtained by studying a subject on a controlled diet containing a known amount of the substances that are to be measured in the excreta. With the diet described, there occurs no alteration of the curve of the output of phosphorus or of the alkaline tide. In table 8 it can be noted that the excretion of calcium through the urine is fairly constant from day to day. The amount of calcium excreted in the feces depends on the amount of stool passed in one day. Calcium is one of the main constituents of feces and one of the factors controlling the contents and consistence of it. As a rule, the amount of the calcium in the feces is ten to twelve times that in the urine. The intravenous injection of the solution of phosphate does not affect the amount of calcium excreted in the stool. When additional calcium is



taken orally it is immediately reflected by a considerable rise in excretion of calcium, in both urine and feces (table 9). This added calcium apparently is excreted within twenty-four hours, as the excretion for the following day is not above the normal. The oral administration of calcium produces a mild increase in the level of serum calcium.

The daily output of inorganic phosphorus in urine, when the subject was on the diet, ranged from 646 to 864 mg. The total amount of phosphorus in the feces depends somewhat on the amount of stool passed but is always less than the amount of phosphorus taken orally and much less than the amount excreted in the urine. The ratio of the total amount of phosphorus in the feces to the urinary inorganic phosphorus is found to be from 1.25 to 1.29. This is not affected either by the injection of phosphorus or by the administration of additional calcium by mouth. The intravenous injection of the solution of sodium phosphate produces an increase of phosphorus both in the urine and in the feces. There is an immediate increase in the output of the phosphorus in the urine. The injected phosphorus is excreted within twenty-four hours or less, for on the following day the output is normal. However, part of the injected phosphorus apparently is lost. This probably occurs through absorption into the tissues and does not amount to more than from 6 to 12 per cent of the amount injected.

The total amount of phosphorus in the feces is increased after injection but is less than that which is taken

orally in the food. One cannot say whether the increased amount of phosphorus is due to excretion from the blood, or whether the absorption from the intestine is inhibited because the level of phosphorus in the blood is so high. The feces were passed from four to five hours after injection of the phosphorus and must have been fairly low in the intestinal tract at the time of injection. Thus it would appear that the increased amount of phosphorus in the feces was due to excretion from the overlaid blood. When the work of Bergmann is considered it must be admitted that some excretion probably does occur. He found, after subcutaneous injection of solution of sodium phosphate, that in carnivora all the injected phosphorus appears in the urine even though the intestine is laden with calcium, in herbivora, on the other hand, the injected phosphorus is excreted almost entirely through the feces. Man, an omnivorous animal, should show some of the characteristics of both and thus should be able to pour phosphorus from the blood into the intestine, especially when the blood is laden with phosphorus in a diffusible form.

It has been suggested in cases of retention of phosphorus that oral administration of calcium would cause excretion of additional amounts of phosphorus through the stool and thus the phosphorus which the diseased kidneys could not excrete would be eliminated. Boyd has shown since that treatment with calcium in cases of nephritis in no way affects the elimination of phosphorus. The ingestion of calcium chloride does not

affect the levels of phosphorus in either urine or blood. The curve of urinary output of inorganic phosphorus retains the same shape it had when the subject was receiving the diet only. The ingestion of calcium chloride for two successive days does not produce a perceptible change in the excretion of phosphorus in either the urine or the feces over a period of twenty-four hours (table 9). The total amount of excreted phosphorus is the same as that when neither calcium nor phosphorus was administered. The ratio of the total amount of phosphorus in the feces to the total amount of inorganic phosphorus in the urine (1.3) is not materially altered from the normal. The intravenous injection of phosphorus following ingestion of calcium chloride produced a mild laxative action. In this instance the intestine was loaded with calcium at a time when the level of inorganic phosphorus in the blood reached the extremely high point of 9.09 mg in each 100 cc. It would be expected that this phosphorus could be removed easily for it is in a very diffusible form. This state, it would seem, would make it adaptable to the influence of the calcium in the bowel, the effect of which would be to draw the phosphorus to the intestine. The results one would think, should be reflected in a very marked increase in the excretion of phosphorus in the feces, with the increase of the amount in the urine not as great as that which occurred when only phosphorus was given. These phenomena did not appear. In table 9, it is shown that the largest amount of the injected phosphorus appears in the urine. The

amount of inorganic phosphorus that is excreted, above the normal amount, is almost as much as the amount injected. There does occur a decided increase in the total amount of phosphorus in the feces but no more than would occur if only phosphorus were given. The ratio of the total amount of phosphorus in the feces to the amount of urinary inorganic phosphorus, which on one day was 1.24, is not remarkably lower than that which was obtained on days when only the phosphorus was administered. There is no suggestion in these results that the calcium in the intestine draws any more phosphorus to it even when the blood is laden with phosphorus above a normal level. Therefore, if these results are true, one can say that the ingestion of calcium does not alter the path of excretion of phosphorus in cases of retention of phosphorus, and the calcium does not have therapeutic value in cases of nephritis from that standpoint.

It has been previously stated that in the normal person the level of inorganic phosphorus in the plasma is the same as that or lower than that in the cells. Also, in cases of retention of phosphorus due to nephritis the level in the plasma is higher than that in the cells. It has been shown that the injection of a solution of phosphate intravenously into a normal subject produces a marked rise in the levels of inorganic phosphorus in the blood. The greatest increase occurs in the level in the plasma, which becomes higher than the level in the cells and retains this position until the levels approach normal. The injection of phosphorus seems to have

no effect on the level of calcium in the serum. The carbon dioxide combining power of the plasma does not diminish after the injection of phosphorus. In fact, there is a tendency toward an increase. This was found to be true, also, in cases of nephritis, whether or not it is associated with retention of phosphorus and acidosis. The significant fact is that reduction of the alkali reserve does not occur.

Studies on the normal subject have shown that the increase in the level of phosphorus in the blood is reflected in an immediate and very prominent increase in urinary excretion of inorganic phosphorus. The peak of excretion occurs within the first hour. This is followed by a gradual fall in output, which approaches normal after four hours. The amount of phosphorus excreted in a fasting subject between the hours of eight and twelve in the morning would be fairly constant from day to day. The figure thus obtained could be subtracted from the amount of phosphorus excreted after injection of solution of phosphate under the same circumstances. The difference, in milligrams, would give an indication of the amount of injected phosphorus that was recovered. The amount recovered would depend on the renal function and would offer some idea of the amount of injury to the kidney, if the return were less than that obtained in the normal subject. About 50 per cent of the phosphorus injected is recovered within four hours, in a normal subject. Excretion of phosphorus is diminished in renal disease. A résumé of the amounts re-

covered in all the cases is given in table 10. A striking feature is the parallelism which occurs in cases of severe nephritis between the return of phenolsulphonephthalein and of phosphorus. As the phenolsulphonephthalein approaches normal, the return of phosphorus remains a little lower. The results would indicate that a return of from 40 to 50 per cent of phosphorus is to be expected from a normally functioning kidney. A return of less than that is indicative of renal injury, the less the return, the greater the injury. The patients (cases 6, 8, 10, and 11) in whom the return of phosphorus was less than 20 per cent died within four months. It is also to be noted in figures 3 and 4 that in cases of severe nephritis the peak of urinary excretion of phosphorus after injection does not occur during the first hour as in the normal subject but is delayed for from one to three hours. It can be concluded from these results that in cases of nephritis the recovery of injected phosphorus depends on the extent of renal injury, and that the urinary response to injection of phosphorus is much delayed when renal function is very low.

#### SUMMARY

Studies were made of the levels in the blood and of the urinary excretion of inorganic phosphorus in the normal person and in subjects with nephritis. A solution was made of the acid and alkaline sodium phosphates and this was balanced to a hydrogen-ion concentration close to that of the blood. This solution was very satisfactory for intravenous injection into dog and man, subjective effects were not noted. The path of

excretion of phosphorus was studied by administering to a normal subject a controlled diet which contained a minimal and known amount of mineral. The daily total amount of phosphorus in the feces and the amount of inorganic phosphorus of the urine were determined. The effect of intravenous injection of the solution of phosphate on the levels of phosphorus in the blood or the amount excreted in feces and urine was studied. In addition, the effect was noted on the levels of calcium in the blood, on the amount of calcium excreted, and on the acidity of blood and urine. Calcium chloride was given orally in doses of from 4.5 to 5.0 gm to determine if calcium altered the path of excretion of phosphorus in any way. It was concluded that calcium does not draw any phosphorus from the blood into the intestine, even when the blood is laden with phosphorus. A standardized dose (6.6 mg for each kilogram of body weight) of phosphorus was injected into a healthy subject and into patients with nephritis to determine how much of the injected phosphorus would be recovered in the urine within four hours after the injection. It was discovered that in subjects with normal renal function, the return was 50 per cent or more. In the presence of renal injury, the return was lessened depending on the amount of injury to the kidney.

#### CONCLUSIONS

1 In a normal, fasting individual the level of inorganic phosphorus in the plasma is equal to or less than the level in the whole blood. In patients with nephritis in whom there

is retention of phosphorus the level of inorganic phosphorus in the plasma is greater than that in the whole blood.

2 Retention of phosphorus associated with retention of creatinine in patients with chronic nephritis offers a fatal prognosis.

3 A mixture of solution of acid sodium phosphate, 9 per cent, and of solution of alkaline sodium phosphate, 9.6 per cent, in a ratio of three parts of the former to seventeen parts of the latter is suitable for intravenous injection into man. It is nontoxic. The intravenous injection of this solution produces an immediate rise followed by a gradual fall in the inorganic phosphorus of the blood, the level of phosphorus in the plasma is greater than the level in the cells, it causes an increase in the amount of inorganic phosphorus excreted in the urine and in the amount of phosphorus excreted in the feces, the amount in the urine is much greater than that in the feces. The carbon dioxide combining power of the plasma, the level of serum calcium, and the amount of calcium excreted in the feces are not appreciably affected by injection of the solution of phosphate.

4 In the normal, fasting subject 50 per cent of the injected phosphorus is recovered in the urine within four hours. In cases of nephritis, the urinary response is delayed and the amount of phosphorus recovered is decreased as the amount of renal injury is increased. Also, the return of the level of inorganic phosphorus in the blood to that preceding injection

is slower in patients with nephritis than in the normal subject

5 In a normal person more phosphorus is excreted in the urine than in the feces. The ratio of the total amount of phosphorus in the feces to the amount of inorganic phosphor-

us in the urine is between 1.25 and 1.29 inclusive. The path of excretion of phosphorus is not altered by the ingestion of calcium chloride even though the level of inorganic phosphorus in the blood is raised through intravenous injection of solution of phosphate.

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# The Long Interval Versus The Short Interval Treatment Of Hay Fever

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A REVIEW of the great volume of work that has been done since Wolf Eisner suggested that the symptoms of Hay Fever resembled the phenomena of experimental anaphylaxis, discloses the fact that we today are confronted with some of the same problems that baffled the pioneers in this study, to-wit

- 1 Is Hay Fever a manifestation of anaphylaxis?

A number of workers including Dunbar,<sup>1</sup> Koessler,<sup>2</sup> Hall,<sup>3</sup> Alexander,<sup>4</sup> Parker<sup>5</sup> and Huber<sup>6</sup> support this view, while in direct opposition are listed the findings of Coca,<sup>7</sup> Cooke,<sup>8</sup> Grove and Coca,<sup>9</sup> Black<sup>10</sup> and Black and Moore<sup>11</sup>

- 2 In group reactions of pollens does desensitization with the predominant member of the biologic group causative of the seasonal attack, protect against all members of that group?

Cooke and Van der Veer,<sup>12</sup> Scheppegrell<sup>13</sup> and Goodale<sup>14</sup> affirm this statement. Their contention is that the chief proteins of the pollens of one group are identical and that the symptoms are produced by contact with that protein. To further support this view Wells and Osborne<sup>15</sup> proved that when tested anaphylactically the chem-

ical relationship of similar tissues of a group parallel the biologic relationship Brown,<sup>16</sup> Watson and Kibler<sup>17</sup> and Bernton<sup>18</sup> take exception to this view. They agree that a certain amount of specificity exists, but contend that this conception does not explain satisfactorily many observed irregularities

- 3 What is the best extraction medium in the preparation of pollen antigen?

The variance of opinions is best demonstrated by a review of the different methods. Noon and Freeman<sup>19</sup>, credited as the first to devise a method of desensitization against Hay Fever, prepared their solution by alternately freezing and thawing the pollen in distilled water. After filtration the extract was boiled in sealed tubes. Clowes<sup>20</sup> precipitated pollen with acetone. Lowdermilk<sup>21</sup> substituted physiologic sodium chlorid solution for the distilled water. Clock<sup>22</sup> used a fluid consisting of 33 1/3 per cent saturated sodium chlorid and 66 2/3 per cent glycerole. Koessler<sup>2</sup> used an 8.5 per cent solution of sodium chlorid and he sometimes precipitated with 95 per cent alcohol, 10 times the volume of the pollen. Goodale<sup>14</sup> soaked grains in water for a few hours and added alcohol sufficient to make the dilution

from 13 to 15 per cent by volume Walker<sup>23</sup> used 12 per cent alcoholic solution Rackermann<sup>21</sup> added to physiologic sodium chlorid a slight amount of alkali in the form of 1 per cent normal sodium hydroxid Coca<sup>25</sup> also utilized an alkali medium, consisting of sodium chlorid and sodium bicarbonate in such concentration that 10 cc of the final fluid equaled about 3 cc of a N/10 alkali Duke<sup>26</sup> modified Clock's method by substituting Cocoa's solution for the saturated sodium chlorid solution All extracts were sterilized by passage through Berkefeld filters Phenol, trikiesol and glycerol were employed to preserve the potency and maintain the sterility of these extracts

- 4 What is the method of choice in the preseasonal desensitization against Hay Fever?

Walker's schedule of treatment has been followed with slight modification by most workers This method consists of determining the threshold of reactivity by testing cutaneously with various dilutions of the causative pollen, viz, 1 10,000, 1 5000, 1 1000 and 1 500 In the average case the patient would react with a 1 5000 or a 1 1000 solution Treatments would begin with the dilution next to that which gave the last reaction, giving 2, 4 and then 6 minims of each dilution at 5 or 7 day intervals until the maximum dose of 6 minims of the 1 500 solution were given Duke<sup>26</sup> further modified this method by administering pollen extracts once or twice a day for the lesser concentrations and continuing at 24 to 48 hour intervals, governed solely by the degree of local re-

action following the preceding dose This method has aroused considerable interest.

The presented study was undertaken for the purpose of determining the relative value between what shall hereinafter be referred to as the long interval treatment advocated by Walker, and the short interval treatment reported by Duke In addition some of the findings in this series may add weight to the evidence for or against some of the uncertainties heretofore enumerated

With this purpose in mind patients presenting themselves for treatment of the Fall type of Hay Fever in May or June were started on the long interval treatment, while those who reported on June 20th or thereafter received the short interval type of treatment Members of both groups were tested with two commercial diagnostic pollen preparations Positive reactions to various members of the compositae family were obtained in all cases of clinical Hay Fever These reactions occurred with about equal intensity with both of the preparations For the long interval treatment an aqueous solution was used in dilutions of 1 10,000, 1 5000, 1 1000, 1 500 and 1 100 After determining the threshold of sensitivity by the dilution tests, 2, 4 and 6 minims of each dilution were administered, terminating the treatment with 6 minims of the 1 100 solution Glycerolated pollen antigen was administered in the group receiving the short interval treatment This is a 66  $\frac{2}{3}$  per cent glycerol and 33  $\frac{1}{3}$  per cent saturated sodium chlorid preparation consisting of 15 individual doses, with 2  $\frac{1}{2}$  units in the



first dose and ending with 3000 units in the 15th dose \*

The comparative results given by the two types of antigen are shown in Charts A and B

A comparison of Charts A and B shows that although the short interval treatment was begun from one to four weeks later, an average of 17 doses was administered against an average of 13 plus doses. Using a glycerolated pollen antigen preparation, the initial dose was  $2\frac{1}{2}$  units. A maximum of 3000 units was reached by rapid increases. This dose may be repeated, if indicated, at 4 day intervals as is shown in cases 3 and 11. Very little difference in the degree of local reactions and no constitutional symptoms resulted in those receiving the short interval treatment, while within 5 minutes following the prescribed injection of pollen, two patients in the long interval group developed angioneurotic edema with shortness of breath, wheezing, etc.—true bronchial asthmatic attacks requiring the administration of epinephrin to overcome the reaction. The results in spite of the short series are very encouraging. Excluding all patients that had more than an occasional sneeze 5 (41+ per cent) were practically free from symptoms. Omitting all patients except those having

Better results are obtained when Hay Fever sufferers who have a bronchitis or who give a history of previous attacks of bronchial asthma receive an autogenous vaccine from the nose or sputum, in conjunction with the pollen extracts throughout the period of treatment. This was not done in this series, thereby avoiding conflict in the conclusions to be drawn from the results obtained as to what the beneficial factors were.

an occasional paroxysm of sneezing and occasional itching of the eyes, etc., 4 (33+ per cent) were markedly improved. Three patients (25+ per cent) who still had symptoms of Hay Fever, were at least 50 per cent relieved as compared with previous seasonal attacks. In the long interval group 4 (18+ per cent) were practically relieved of symptoms, 9 (40+ per cent) were markedly improved, 7 (31+ per cent) were improved and 2 (9+ per cent) were failures.

Ephedrin, not used in any cases of this series, has been disappointing in the treatment of Hay Fever. Some relief is obtained before the onset of severe symptoms, but when fully established ephedrin is practically useless. Two factors seem important enough to report.

1 Ephedrin, even in small doses, may have a hypnotic effect in some cases. A child of 5 years of age was given  $1/32$  of a grain every 3 hours. After 3 doses the child slept an unusual number of hours. This effect may be due to impurities in the preparation of the drug.

2 There is a rapid development of tolerance to the drug. The same child, using the same tablets, could in one month take  $\frac{1}{2}$  gram of ephedrin without relief or untoward symptoms.

Recapitulating. Excellent results were obtained in 74 plus per cent of cases in series A with no absolute failures, while in Series B satisfactory results were obtained in 59 plus per cent with two failures. Koessler<sup>23</sup> in 1914 reported 36 cases of hay fever treated, of which 11 plus per cent were entirely relieved and 22 plus per cent were failures. Walker<sup>25</sup> in 1921 reported 22 per cent of a series of 202 cases entirely relieved of symptoms and 6 plus per cent failures. Cooke and Van der Veen<sup>26</sup> reported

CHART "A" (Therapeutic)  
Short Interval Treatment

Patient	Sex	Treatments		Number of Treatments	Interval	Z Reactions		95-100	80-95	50-80	50% & less
		Began	Ended			Local	General				
1 J F	M	July 1	Aug 16	30	Daily	1-2+	None	X			
2 B Y	F	Aug 1	Aug 16	15	Daily	1-2+	None	X			
3 W F	M	July 20	Aug 16	18	1-4 days	1-2+	None			X	
4 A F	F	July 20	Aug 16	18	1-4 days	1+	None	X			
5 M K	M	Aug 1	Aug 15	15	Daily	1-3+	None	X			
6 P D	M	Aug 1	Aug 15	15	Daily	2-3+	None		X		
7 G D	M	July 20	Aug 14	15	1-2 days	2-3+	None		X		
8 J G	M	July 25	Aug 14	15	1-2 days	2-3+	None		X		
9 A N	F	July 28	Aug 14	15	Daily	3+	None		X		
10 C M	F	Aug 1	Aug 16	15	Daily	1-2+	None			X	
11 R L	F	July 24	Aug 15	18	1-4 days	1-2+	None	X			
12 A B	F	Aug 1	Aug 15	15	Daily	1-2+	None			X	

5 or 41+%  
4 or 33+%  
3 or 25+%

Remarks

- Case 1 had 15 daily doses ending July 16 and 15 additional doses ending August 16
- Case 3 had daily doses for 15 days followed by 3 maximum doses at 4 day intervals
- Case 7 omitted a day occasionally when local reactions had not subsided
- Case 11 had 15 daily doses then the maximum dose every 4 days for 3 doses
- Lederle's Glycerolated Pollen Antigen used in this group

Chart "B" (Therapeutic)  
Long Interval Treatment

Patient	Sex	Treatments		Number of Treatments	Interval	Z Reactions		General	95-100	80-95	50-80	50% & less
		Began	Ended			Local	None					
1	FO	M	June 15	Aug 16	5 days	1-2+	None				X	
2	FD	F	June 15	Aug 16	5 days	1-2+	None		X			
3	FK	F	June 1	Aug 14	5 days	1-3+	None		X			
4	LO	M	June 5	Aug 15	5 days	1-2+	None			X		
5	MO	F	June 15	Aug 18	5 days	1-3+	None			X		
6	CH	F	June 5	Aug 16	5 days	1-3+	None				X	
7	BU	M	June 10	Aug 18	5 days	1-3+	None		X			
8	SS	F	June 15	Aug 15	5 days	1-2+	None					X
9	MF	F	June 15	Aug 15	5 days	1-2+	None			X		
10	HJ	F	June 10	Aug 15	5 days	1-4+	Ang Neu Edema Br Asthma				X	
11	JS	M	June 12	Aug 15	5 days	1-2+	None				X	
12	IL	M	June 15	Aug 15	5 days	1-2+	None				X	
13	BL	F	June 12	Aug 18	5 days	1-4+	Ang Neu Edema Br Asthma			X		
14	HS	M	June 15	Aug 15	5 days	1-2+	None					X
15	HB	M	June 14	Aug 15	5 days	1-2+	None		X			
16	HO	F	June 15	Aug 15	5 days	1-3+	None					
17	AM	M	June 20	Aug 17	5 days	1-3+	None			X		
18	RR	M	June 18	Aug 15	5 days	1-2+	None			X		
19	AD	F	June 16	Aug 15	5 days	1-2+	None			X		
20	CC	F	June 14	Aug 15	5 days	1-2+	None			X		
21	CA	F	June 18	Aug 14	5 days	1-3+	None				X	
22	PO	M	June 15	Aug 16	5 days	1-2+	None				X	

4-18+% 9-40+% 7-31+% 2-9+%

Arlington Chemical Company's aqueous solution used in this group  
Z

One plus—An erythema or wheal approximately 1/2 centimeter in diameter  
Two plus—Same as one plus except - centimeter in diameter  
Three plus—Same as one plus except 1 1/2 centimeters in diameter  
Four plus—Same as one plus except 2 centimeters or more in diameter

1,774 patients treated between 1916 and 1920—25 per cent were entirely relieved and 10 per cent were failures. The results obtained in series A with glycerolated pollen antigen compare favorably with the report of Clock<sup>29</sup> who obtained relief of symptoms in 84 per cent of 1,578 cases, using a similar preparation.

The foregoing indicates that a staple pollen antigen is requisite to the best results. The increased efficiency of our present day methods in preseasonal desensitization is due to two factors:

- 1 The marked increase in the concentration of a pollen content.

This can readily be seen by the fact that only 3 years ago, the maximum dose of commercial water soluble pol-

len protein was a 1:500 solution. These commercial houses as a routine now advise 1:100 solutions as a maximum dose. Those firms marketing a glycerolated pollen solution sell a preparation containing 3,000 to 4,000 pollen units as their maximum dose, as against 1,000 units of a few years ago.

- 2 The increased stability of glycerolated pollen antigen.

This was shown by Clock who found no loss of complement binding capacity in his preparation after 14 months. Beinton corroborated this finding and further proved that evidence of clinical potency is no indication of the original activity of the preparation. Using his own alcoholic saline pollen solution, comparing same with glycerolated pollen antigen pre-

CHART "C" (Etiologic)  
Short Interval Treatment

Patient	Age of Onset	Age First Seen	Heredity	Operations for Hay Fever*	Complications
1 J F	15	23	Asthma	2	Br Asthma
2 B Y	40	50	Hay Fever	1	
3 W F	58	61			
4 A F	49	51	Asthma		
5 M K	19	23	Asthma		
6 P D	36	49			Br Asthma
7 G D	31	51	Asthma		Br Asthma
8 J G	24	31	Asthma	2	Br Asthma
9 A N	43	51			
10 C M	28	36	Asthma	1	Br Asthma
11 R L	20	24	Asthma	2	
12 A B	15	35	Asthma Eczema		Br Asthma
Average	31+	40+	9 or 74+%	5 or 41+%	6 or 49+%

\*No benefit derived from the operation

pared by the method of Clock, he found that his preparations showed a marked loss of antigenic properties, tested by the complementing fixation method as devised by Clock, after a period of 4 months while the glycerolated pollen antigen retained its original antigenic properties

A composite form of the charts shows that 9 cases of series C and 7

cases of series D, a total of 16 cases (47+ per cent of the entire series), gave a history of some form of allergy, including Hay Fever, Asthma, Urticaria and Eczema in some direct antecedent Six cases of series C and 9 of series D gave a history of attacks of Bronchial Asthma during previous seasonal attacks These facts plus the occurrence of angio-neurotic edema

CHAR1 "D" (Etiologic)  
Long Interval Treatment

Patient	Age of Onset	Age First Seen	Heredity	Operations for Hay Fever*	Complications
1 FO	30	61			
2 ED	34	46	Asthma	2	
3 FK	38	42	Hay Fever		Br Asthma
4 LO	2	6		1	
5 MO	40	44			
6 CH	14	18			Spring and Fall Type
7 BU	28	34	Hay Fever	1	Br Asthma
8 SS	27	28	Asthma		Br Asthma
9 MF	15	36			
10 HJ	24	27			Br Asthma
11 JS	23	36	Hay Fever		Spring and Fall Type
12 LL	26	46		1	Br Asthma for 40 years
13 BL	15	23	Asthma	2	
14 HS	30	41			
15 HB	18	33			Spring Type Urticaria
16 HO	19	23			Br Asthma
17 AM	34	36			Br Asthma
18 RR	12	22			
19 AD	35	48	Asthma	1	Br Asthma
20 CC	39	44			Br Asthma
21 CA	34	39			
22 PO	26	61		1	
Average	25+	36+	7 or 31+%	7 or 31+%	9 or 40+%

\*No benefit derived from the operation

CHART "E"  
Composite of Charts "A, B, C and D"

	Sex		Average Age		Duration	Fam Hist of Allergy	History of Asthma Complicating Previous Seasonal Attacks	History of Nasal Operations For Relief*
	M	F	Onset	First Seen				
Series A								
(12) C	6	6	31+	40+	9+ years	9 or 74+%	6 or 49+%	5 or 41+%
Series B								
(22) D	10	12	25+	36+	11+ years	7 or 31+%	9 or 40+%	7 or 31+%

\*No benefit derived from the operations

†All cases reacted to Ragweed, short and Ragweed, giant. In addition they reacted to one or more of the following pollens: goldenrod, sunflower, Russian thistle, cocklebur, yellow dock and corn.

and Bronchial Asthma in two cases following therapeutic injections of pollen as noted on Chart B, make it difficult to separate Hay Fever from the category of anaphylactic conditions. It is noteworthy that, although all the cases reacted to many members of the composite group productive of the fall type of Hay Fever and in spite of the fact that all the groups were treated with the combined Ragweed, short and giant Ragweed pollen, the results have been excellent. It therefore appears that treatment with the predominant member of the biologic group, especially if the predominant member gives the predominant reaction, will suffice for the treatment of seasonal Hay Fever. It will be observed that 12 cases (35+ per cent of the entire series) gave a history of one or more nasal operations that were performed to relieve their Hay Fever without a single instance of benefit resulting therefrom. It appears then that operative work without an abso-

lute indication other than Hay Fever is a useless procedure.

*Comment.* The short interval treatment of Hay Fever has many advantages.

(a) Desensitization can be established within a relatively short period, two or three weeks. This statement must be modified, for the peak of pollenation is so great in some localities that weekly treatments throughout the season, with the maximum dose, seems advisable in order to obtain the best results. Dike and Durham<sup>30</sup> have shown a wide variability in pollen concentration in various cities, which justifies this procedure. They have shown that the count of pollens at the peak of the ragweed season in Chicago in 1925 was 500 pollens covering an area of 55/100 square inch, while in Kansas City it reached the tremendous number of 4,500, and in Oklahoma City, 7,200. These findings demonstrate the necessity of accurate knowledge of the pollenation curve for the

proper management of Hay Fever sufferers in any community. In New York City the maximum rarely reaches above 100 pollens per 55/100 square inch. Therefore, I deem it unnecessary to continue treatment after the onset of the season, except where the patient was not sufficiently desensitized prior to the season, or in the case of a highly sensitive patient, who in previous years had not received complete relief with the aforementioned procedure.

(b) Local reactions following treatments appear greater with the long interval treatment. Some of the wheals assume the proportion of a silver dollar and are accompanied by constitutional symptoms. The local reactions in those receiving the short interval treatment were less severe and in most instances had disappeared sufficiently so that subsequent doses could be given. In no instance in this series was it necessary to omit more than one day because of the local reactions caused by the preceding dose. The reaction usually reached the maximum within 15 minutes and had subsided sufficiently so that the patient was permitted to leave the office in 30 minutes.

(c) The pollen treatment sets used in the season of 1928 were of the same lot as those used in 1927, having been kept in the icebox for the entire

year. The results in 1928 were no different from those in 1927, indicating that there was practically no loss in the potency of the extracts during that period of time.

### CONCLUSIONS

1 The intensive or short interval treatment seems the method of choice in the treatment of Hay Fever.

2 Hay Fever with the hereditary background and the frequent complications of Asthma, Urticaria and Angioneurotic Edema cannot be excluded from the category of Allergic Diseases.

3 Treatment with the predominant member of a biologic group of pollens causative of seasonal Hay Fever, is sufficient to care for the entire biologic group. Where more than one biologic group is present in sufficient concentration to cause symptoms, a combination of the predominant members of such groups is advisable for good results.

4 Best results are obtained with glycerol pollen antigen. This preparation retains complete potency for considerable periods of time.

5 Nasal operations with Hay Fever as a primary indication are worse than a useless procedure.

6 Ephedrin in the treatment of Hay Fever has proven disappointing.

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# Brittle Bones And Blue Sclerae. Report Of A Case With Glycosuria

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THE recognition of the familial occurrence of brittle bones and blue sclerae is credited to Ed-dowes<sup>1</sup>, although this association of abnormalities was reported by Spur-way<sup>2</sup> four years earlier. Later, Bron-son<sup>3</sup> and Van der Hoeve and de Kleijn<sup>4</sup> called attention to the heredi-tary association of otosclerosis and labyrinthine disease with deafness in the affected families. The syndrome is usually transmitted by the female, though it may be transmitted by the male. A number of affected families has been reported, the articles by Bronson<sup>3</sup> and Key<sup>5</sup> are accompanied by extensive bibliographies. Since the latter publication, additional families have been studied by Moller<sup>6</sup> and Paal<sup>7</sup>.

Besides the hereditary occurrence of the syndrome of pathological fractures and blue sclerae, isolated cases have been reported in which no hereditary influence could be elicited from the family of the affected member. Bron-son,<sup>8</sup> Herrman,<sup>9</sup> Ostheimer,<sup>9</sup> Gutzeit<sup>10</sup> and others, and recently, Hein<sup>11</sup> have reported instances of the sporadic ap-pearance of this condition. Hein traced 23 members of a family in four generations without discovering an-other case. The authors' case seems

to belong to this category. Hereditary and non-hereditary cases present the same clinical picture.

## REPORT OF CASE

A girl, aged 4 years, 4 months, was seen April 1, 1929. The complaint was frequent fractures of the bones of the arms and legs.

The family history was essentially nega-tive, except for the fact that a paternal uncle suffered from a neurological condition and had been unable to walk since he was a young man. A normal brother had died at 15 months of age of diphtheria. No other case of brittle bones or blue sclerae had been heard of in the families of the father or mother. Both parents were living and well.

Except for the presence of blue sclerae, the patient had seemed normal at birth, but at six weeks of age the right humerus was fractured. At one year there were multiple fractures of both femurs, and from this time, on an average of every six months, there was a fracture of an arm or leg. Abnor-mality in shape and development of the thorax was first noted at one year. Appe-tite had always been capricious and very poor, and there had been frequent attacks of nausea and vomiting from unknown cause. The first teeth had erupted at eight months. Mentality was normal.

Physical examination. Weight, 22½ pounds (10.2 kg). The patient was unable to walk, but got about upon a small con-trivance with wheels, propelling herself with her feet. The musculature of the extremi-ties was flabby and atrophic. The head was

quite large in proportion to the body, and seemed to rest directly on the thorax. The thorax showed a combination of pigeon-breast and barrel shape, its lower borders resting on the brim of the pelvis. The abdomen was protuberant. There was moderate flexion of the thighs and the legs could not be straightened. The sclerae were deep slate blue in color. The fundi were normal on ophthalmoscopic examination. The teeth were well formed and in good condition. There was moderate hypertrophy of the tonsils. The remainder of the examination revealed normal findings.

**Laboratory examinations.** Red blood cells, 4,020,000, hemoglobin, 70 per cent (Dare), white blood cells 7,750. Differential white cell count: neutrophilic leukocytes, 60 per cent, lymphocytes 28 per cent, monocytes 12 per cent. The stained smear showed a normal picture. The blood Wassermann and Kahn reactions were negative. Serum calcium was determined on three occasions with readings of 13.0, 12.9 and 11.7 milligrams per cent (Clark and Collin's modification of the technic of Tisdall and Kramer), accompanying the last calcium determination the blood phosphorus was 4.4 milligrams per cent (technic of Fiske and Subbarow). The fasting blood sugar was 73 milligrams per cent (venous blood, technic of Folin-Wu), and a simultaneously voided specimen of urine was sugar-free. A 24-hour specimen of urine gave slight reduction of Benedict's qualitative solution, but showed no other abnormality. Specimens of urine collected one or two hours after a meal regularly gave slight to moderate reactions for sugar, while fasting specimens were always sugar-free. The reacting substance reduced Nylander's solution, yielded typical osazone crystals with phenylhydrazine, was dextrorotary in the polariscope, was fermented by yeast and was completely destroyed by fermentation.

As a rough test of glucose tolerance, the patient was given 30.0 gm glucose (about 3.0 gm per kg of body weight) in 200 cc water, with the juice of one lemon. One hour later, the venous blood sugar was 167 milligrams per cent, 32 cc of simultane-

ously voided urine contained 0.2 per cent of reducing substance by Benedict's quantitative method. This reducing substance displayed the same characteristics as that present in postprandial urine specimens, proving the substance to be glucose.

We wished to determine the patient's calcium and phosphorus balance, but were prevented from doing so by an inadequate period of observation and the patient's capricious appetite. Consequently, during a four-day period of unrestricted general diet, total specimens of urine and stool were collected. The average calcium excretion in the urine was 437 milligrams, and in the stool 780.5 milligrams. The average daily excretion of phosphorus was 287.7 milligrams in the urine and 376.0 milligrams in the stool. Determinations were made upon material ashed in a platinum crucible, the technic of the determinations is noted above.

A roentgenological survey of the bony skeleton was made at the Albert Steiner Clinic. The skull is rather round, with a bulging frontal and occipital area. The fronto-parietal suture is closed, while the occipito-parietal is still open. The skull bones are unusually thin, the head having the appearance of the hydrocephalic type. Dentition appears to be progressing normally. The frontal sinuses are not developed as yet. Mastoid cells are just beginning to appear. Sella is normal in size and shape. The chest is short and broad. The mediastinum is wide. The rib interspaces are narrow. Rib angles are acute. The diaphragms are higher than normal. The cervical, thoracic and lumbar vertebrae are narrow, giving the impression of being compressed. The head rests nearly on the shoulders. The body is short. The long bones of upper and lower extremities are not well developed in breadth. Their length is apparently normal, but the bones themselves are long and spindling. The epiphyses appear to be developing normally. The texture of the long bones is that of an atrophic or decalcified type. The cortex is unusually thin, the medulla is wider than normal. Both femurs are bowed outward, the tibiae are bowed inward, due to muscle pull. The right femur presents a deformity due to



FIG 1 Side view of patient, showing large head, very short neck, deep antero-posterior diameter of chest, kyphosis of spine, protuberant abdomen, atrophic musculature of extremities



FIG 2 X-ray showing femurs, tibias and fibulas The convex light area at the top of the figure is produced by the patient's abdomen

multiple fractures followed by union and irregular new bone formation. The shaft of this femur has a rather cystic appearance, with marked trabeculation throughout. The ends of all long bones appear expanded, due to the lack of development of the shafts. The pelvis is greatly deformed, pressure from the femurs having pushed the internal surfaces of the acetabular parts nearly in apposition. This giving way of the pelvis has occurred at the lines of epiphyseal union between the lower half and the ileum. There is more atrophy of disuse in the thigh and leg bones than there is in the forearm and arm. None of these bones have the appearance of rickets, scurvy, or syphilis. The carpals and tarsals are poorly developed, as are the phalanges, metacarpals and metatarsals.

#### DISCUSSION

The excretion of glucose has not been noted in other cases of brittle bones and blue sclerae. In our patient it probably represents a coincidental anomaly. Our investigation was necessarily too incomplete for an exact explanation of the mechanism of the glycosuria. However, it may reasonably be assumed in the presence of a normal fasting blood sugar and a normal blood sugar rise one hour after a relatively large dose of glucose, and in the absence of any clinical symptoms of diabetes, that the glucose excretion represents a benign condition, probably the result of a low renal threshold.

Estimations of chemical constituents of the blood have been made in only a few instances. In Key's patient, the hydrogen ion concentration of the blood was pH 7.58, the serum calcium was 12.17 milligrams per cent and the blood phosphorus was 4.06 milligrams per cent. In three of Paal's cases the serum calcium readings were 9.06, 9.99, and 12.8 milligrams per cent, re-

spectively. Including the observations in our case, one may say that the serum calcium may be normal or slightly elevated, while the blood phosphorus is practically normal.

Calcium, phosphorus and nitrogen balance studies have been carried out in a few cases of osteogenesis imperfecta, the results of these studies have not displayed a constant abnormality. So far as we are aware, no studies of this type have been undertaken on patients with brittle bones and blue sclerae, except by Key. The balances of his patient were determined in two six-day periods, but the results were never published. In our case, the estimations of the distribution of calcium and phosphorus in the urine and stools showed a greater percentage of both constituents in the stool than is normal. The relative proportions of calcium and phosphorus in the stool were almost the same as in calcium phosphate, which suggests the possible formation of an insoluble calcium compound which cannot be absorbed from the bowel.

The blue color of the sclerae is explained by the majority of authors as an abnormal transparency of the sclerotic coat of the eye which permits the blue uvea to show through. Histologic examination of the affected eye was made in one of Brinson's patients. Other anomalies of the eye have been noted particularly the presence of embryotoxon in both hereditary and sporadic cases.

The acuity of hearing was normal in our patient. Authorities agree that deafness first appears in early adult life, or later.

The physical characteristics of af-

affected individuals vary, as noted in the descriptions of different authors. The patients are usually small and slender, but two of Key's cases were somewhat obese. The head may be normal in size and shape or show tronto-occipital elongation or an exaggeration of the shape noted in rickets. The fontanelles may remain open for years. There is often deformity of thorax and spine and there may be bowing of the extremities.

Roentgenographic examination of the skeleton displays changes in the skull, the vertebrae and long bones. The sites of previous fractures may show much or little callus. The cortex of the bones may be quite dense, while other portions of the bones cast very faint shadows. Key discusses these changes in detail.

Key gives the only gross and histologic description of excised bone. Hein reports an autopsy on his patient who had multiple fractures at birth, and died of pneumonia at five months of age. The examination revealed fractures of the bones of the skull. No histologic report of the bones is presented.

Nearly all authors call attention to the fact that while fractures result from the slightest trauma, they are usually painless, repair very rapidly, and often leave no deformity.

There is general agreement that the anomaly of brittle bones and blue

sclera is due to a hereditary hypoplasia of the mesenchyme.

Treatment can be empirical only in a condition which is so poorly understood. Sunlight, a balanced nourishing diet with sufficient fresh milk to yield an adequate calcium and phosphorus intake, cod liver oil preparations, and ultra violet radiations, constitute rational hygienic therapy. In addition, our case is consuming a quantity of lactose each day, in the hope that it may promote the absorption of calcium and phosphorus from the intestinal tract by virtue of its acid producing effect. Orthopedic procedures are often indicated. Affected individuals may die from intercurrent infection. As puberty and young adult age is reached there is often spontaneous improvement with a greatly reduced liability to fracture.

#### SUMMARY

A sporadic case of brittle bones and blue sclerae is reported. The clinical picture conforms to cases previously described. In addition, an apparently benign glycosuria is present. Serum calcium determinations gave figures at the upper limits of normal, or slightly above. Estimations of urine and stool calcium and phosphorus gave evidence of abnormally high percentages of both in the stool, in such proportions as to suggest the possibility of faulty absorption from the intestinal tract.

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# Argyll-Robertson Pupils In Polyneuritis. Report Of And Theoretical Deductions\*

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Argyll-Robertson pupils developed in the toxic polyneuritis. The subsidence of the disease was recorded for two years. Their presence in the wrong diagnosis, as a part of the path-

om chronic carcinoma and chronic in six months. Iritis in the second stage of the disease, optic neuritis, bilateral fameningeal irritation (spinal fluid), neuritis (spinal fluid) for nine days, the normal

le paper, Sven Nilsson, the anatomy of the afferent and efferent pupillary nerves, the most important in Argyll-Robertson

Sanitarium Clinic

The afferent pupillo-motor fibers arise in the retina and are most strongly concentrated at the macula lutea. In the optic nerve, chiasm, and optic tract the fibers are superficially placed, in the tract they lie in their respective fields of vision. At the level of the lateral geniculate bodies, the pupillo-motor fibers leave the tract, converge, running medially through the brachia of the corpora quadrigemina anterior. Some fibers enter this body, but a compact bundle runs into the dorsal part of the posterior commissure in which it crosses to the other side. It then runs in the descending part of the posterior commissure ventrally to the oculomotor nucleus. Throughout their course in the posterior part of the optic tract and over the superior colliculus, the fibers are extremely superficially placed.

As the case to be presented was free from syphilis, we are interested in all possible causes of Argyll-Robertson pupils. In enumerating the "most important" causes, Ingvar names 1, syphilitic processes, 2, disseminated sclerosis, 3, polioencephalitis superior of Wernicke, 4, epidemic encephalitis, 5, severe chronic alcoholism, 6, diabetes



mellitus, 7, sulphide poisoning, 8, severe traumatism of the skull, and 9, tumors and pathological processes in the region of the anterior corpora quadrigemina. Fuchs<sup>2</sup> states that 10, lead poisoning, and 11, tobacco poisoning may cause reflex immobility, while Mooie<sup>3</sup> describes the condition as an occasional 12, congenital manifestation. He also states that Argyll-Robertson pupils may occur as a result of 13, syringobulbia. He quotes Kinnier Wilson as ascribing the condition to 14, diffuse toxic-infective states. We have seen a case (reported elsewhere<sup>4</sup>) in which 15, no cause could be determined and which progressed through the Argyll-Robertson stage to complete ophthalmoplegia interna, but with development of pupillary contraction whenever the patient swallowed anything.

While theories concerning reflex immobility of the pupils are numerous, all heretofore have failed to explain every phase of the phenomenon, and all have failed to explain every case on record. The demonstration of Ingvar, however, seems quite convincing and the occurrence of Argyll-Robertson pupils in the present case, (apparently a unique one), is in entire harmony with this latest account of the pathology of reflex immobility.

Ingvar agrees with Kinnier Wilson<sup>5</sup> and others that the lesion is in the afferent side of the reflex arc. Wilson states that the lesion may be anywhere along this arc up to the synapse of the pupillo-motor reflex fibers with the pupillo-constrictor center in the third nerve nucleus or its vicinity. But Ingvar is more specific in defining the

pathology as a marginal destruction within the basal subarachnoidal spaces of the brain. The pupillo-motor fibers have already been followed through this very area (optic nerves, chiasm, optic tract, superior corpora quadrigemina). He says, 'We have to look for the pupillo-motor pathways on the surface of the diencephalon. We know for certain that they take a surface route from the posterior part of the optic tract to the anterior (posterior) commissure in front of the anterior quadrigeminal bodies. As the metatubercular and tubercular meningitic processes produce successively developing marginal degenerations of the optic pathways as also of the diencephalic parts on the whole, the pupillo-motor pathways must be injured at an early stage.'

The reflex immobility of the pupil is to be considered simply as a meningitis symptom. As all the evidence indicates that *only such morbid processes as manifest themselves in producing marginal destructions within the basal subarachnoid spaces of the brain are able to cause the Argyll-Robertson pupil*, (the italics are ours), we understand that the metatubercular and tubercular diseases hold a monopoly among the causes of this valuable clinical symptom. The case here presented, while apparently unique as an occurrence, nevertheless is easily understood on the basis of the above pathology and thus corroborates the interpretation of Ingvar.

#### REPORT OF THE CASE

A man of 62 years, whose family history was not noteworthy, came complaining of pain and weakness in the legs. Of childhood disease, he had

had only diphtheria which had left him with weakened muscles of the throat. Aside from this, he had had no serious illness until he suffered an attack of appendicitis in 1924, following which he had developed a colon bacillus cystitis and bilateral pyelitis.

In the summer of 1928, he had experienced no urinary trouble for over a year, when he suddenly developed pains and stiffness in the arms followed by a marked weakness. This progressed until he was unable to comb his hair or raise even a cup to his lips. After some weeks he recovered. (During his illness he was examined by Drs. Crane and Jackson of Kalamazoo, Mich., whose complete records were kindly placed at our disposal and which show definitely that the patient's pupillary reflexes were entirely normal prior to his consulting the present writers.)

March 15, 1929, the patient developed severe pains in his legs followed by weakness. This progressed until he was able to stand only if his knees were set straight, but if they bent he would sink to the ground. On the tenth day, he developed suddenly a paralysis of both sides of his face and four days later he came under the care of one of us. In the general examination, the findings worthy of note were: Blood pressure 180-220 systolic, 100-110 diastolic, widening and tortuosity of the aorta (seen by fluoroscope), heart dulness 11 cm. to the left and 3 cm. to the right of midline, second aortic accentuated, brachial and radial arteries definitely thickened on palpation, much pus in urine, and a trace of sugar in three specimens, none in two others, blood Wasserman negative,

N P N 378, uric acid 3.6, sugar 150 mg. per 100 c.c. of blood, red cells 5,020,000, white cells 8,400, of which polymorphonuclears made up 65% and small mononuclears 35%. The pupils were found to be rigid to light stimulus, but contracted well on convergence. There was a bilateral facial nerve paralysis as shown in Figs. 1 and 2. Abdominal and cremasteric reflexes were absent, sensation was disturbed in the lower extremities below the knees. There was marked weakness as described above.

A neurological examination presented the following (in abstract). The pupils were unequal, right greater than left. Both responded sluggishly to light, the right possibly not at all. Both responded well on convergence. Hearing, smell and taste were unaffected. There was complete paralysis of all muscles supplied by both facial nerves, as a result of which the palpebral fissures were widened. During downward gaze and attempt to close the eyelids, these moved up slightly. During upward gaze, eyeballs and eyelids were both up above the normal (hyperkinetic symptoms due to overaction of unopposed muscles). Pressure pain was diminished on both sides. There was no paralysis of any muscles of the lips or mouth and deglutition was normal. The hand grip registered 70 right and 80 left on the dynamometer. No paresthesias, anesthetics or pains in the arms or hands were found. Abdominal reflexes were absent. All movements of the lower extremities were weakened. Patient could stand if knees were stiffened. All reflexes (superficial and deep) in the lower extremities were absent. There was no



FIG. 1 Argyll-Robertson pupils in polyneuritis



FIG 2 Argyll-Robertson pupils in polyneuritis

tenderness along the nerve trunks and no anesthetics or paresthesias, but considerable pain was present in the lower extremities

Four days later an examination showed that the pupils had become completely fixed to the light reflex. The right was 5 mm, the left 4 mm, both irregular in outline. In addition the arms and hands had become painful and considerably weaker. On the other hand, the right Achilles reflex had returned. There was an absence of vibration sense on the right up to the level of the tenth dorsal segment. On the left this extended only to the third lumbar segment.

Still five days later a re-examination was made, and the striking fact discovered that the pupils responded very readily to light. They were equal in size, regular in outline, and showed no abnormality of any kind. The facial nerves were still completely paralyzed. The arms and hands had become tender, much weaker (R +5, L 35) and an area of hypesthesia had appeared along the ulnar surface of the left hand. A zone had appeared at about the 8th dorsal segment below which sensation to pin prick was diminished and above which it was normal. Another line of demarcation had appeared at about the knee level below which sensation to pin prick was much diminished.

Tests for reaction of degeneration were made on both sides of the face, both forearms and both legs. An incomplete reaction of degeneration was found in all groups tested. The facial nerves were most completely involved

those of the forearm regions next, those of the legs least.

A fundus examination showed a bilateral neuroretinitis, many hemorrhages and exudate near the papillae. There was also a high degree of retinal arteriosclerosis.

A spinal puncture showed 200 mm water pressure, 3 cells per cu mm, globulin 4 plus by the Pandy, plus by the ammonium sulphate method, Wasseimann test negative, sugar 111 mg per 100 cc, Lange colloidal gold curve negative.

From this time no extension of the disease was observed. In two weeks, the patient could walk, a week later upper facial movements began and the eyes closed fairly well. The abdominal reflexes were still absent, but the cremasterics and deep reflexes had returned.

It was obviously important to determine, if possible, whether the optic neuritis was due to the cardiovascular-renal disease or was a part of the general polyneuritis. An examination was made in June, revealing a marked subsidence of the polyneuritis and also of the optic neuritis. The swelling of the nerve heads had decreased from two diopters to one-half diopter and the other manifestations had diminished. There was still considerable involvement of the right facial nerve, little of the left, and considerable weakness remained in the lower extremities. The cardiovascular disease had not diminished. We, therefore, conclude that the optic neuritis came and receded with the general polyncuritis and bore little, if any, relation to the cardiovascular renal syndrome.

## DISCUSSION

When the patient was first seen by us, he had Argyll-Robertson pupils. We found it necessary to consider the patient a syphilitic who had developed polyneuritis. It was learned through a great deal of questioning that the patient had worked in composition shingles (exact chemical composition unknown) just prior to each of the two attacks of polyneuritis, and his pyelonephrosis had been peculiarly quiet during this time. When the pupils became normal, we were suddenly faced with the necessity of explaining the pupillary condition as due to polyneuritis, or the two conditions due to one cause. Kinnier Wilson's statement that reflex immobility may occur in the course of acute toxic-infective states would seem to satisfy us clinically, but not pathologically.

From the pathological standpoint, we considered other explanations. That central neuritis occurs quite frequently in polyneuritis is known and has recently been called to our attention again<sup>6</sup>. In the case presented, we were unable to show evidence of central neuritis above the level of the D8 segment. A non-specific central neuritis in the region of the oculomotor nucleus which caused Argyll-Robertson pupils and nothing else would have

to be assumed to be as specifically selective pathologically as that assumed by some to occur in such pupils when of syphilitic origin. Such assumptions would be entirely speculative. On the other hand we found a bilateral optic neuritis and considerably increased globulin in the spinal fluid. We, therefore, know without assumption that inflammation of the regions traversed by the afferent pupillo-motor fibers was in progress. With the onset of this inflammation, Argyll-Robertson pupils developed, with its subsidence they disappeared. We feel justified in concluding that the case corroborates entirely Ingvar's explanation of the pathogenesis of reflex immobility of the pupils.

## SUMMARY

A case is reported in which during the course of an acute polyneuritis Argyll-Robertson pupils, bilateral optic neuritis, and bilateral Bell's palsy developed. The pupils became normal on the ninth day. Evidence is furnished by the unique case to show that Sven Ingvar's ideas of the pathogenesis of reflex pupillary immobility are probably correct.

The writers are indebted to Dr W H Riley for the first neurological examination and to Dr L V Stegman for the fundus examination.

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# Undulant Fever In Man. Report Of A Case Due To *Brucella Abortus*

By WILLIAM R VIS, M D, *Grand Rapids, Michigan*

**A**BOUT twenty-five years ago<sup>1</sup> attention was directed toward the Island of Malta because of the prevalence there of undulant fever<sup>2</sup> An intensive study proved that goats harbored the disease and that raw goat's milk was capable of transmitting the infection to man<sup>3</sup>

The infecting organism was identified as *Brucella melitensis*<sup>4</sup> and the diagnosis of the infection was simplified by the development of serum agglutination tests<sup>5</sup>

The study of *Brucella melitensis* has not been confined to Malta and adjacent Mediterranean regions but has now embraced grazing areas in every continent In the United States the disease was found to be common in Texas<sup>6</sup> and human infection not unknown<sup>7</sup> An epidemic occurred in Albuquerque, N M, following the importation of goats, and some thirty human cases were recognized within a few weeks<sup>8</sup> Agglutination tests of the goat's serum have proved that these animals were the source of the disease and it has been shown that the organism can be isolated from the milk

Today a new situation confronts us Two other domestic animals have been shown to harbor the *Brucella* type of organism A species of *Brucella* me-

litensis is found in hogs, and human infection by this porcine type is becoming recognized in increasing numbers Even more alarming is the incidence of infection in cattle by a similar organism, *Brucella abortus* More than two hundred human cases have recently been reported as due to bovine or porcine infection 125 cases in Iowa,<sup>9</sup> 50 cases in Michigan, and 91 cases in New York

The differentiation of these species has been made possible largely through the pioneer work of Dr Forrest Huddleson<sup>10</sup> in Michigan, and that of Dr Alice Evans<sup>11</sup> who, herself, became infected with the disease

Three main avenues exist for the transmission of the infection from animals to man

First, cow's milk has been shown to contain *Brucella abortus*<sup>12</sup> The ingestion of raw milk is dangerous

Second, close contact with infected animals may lead to infection This is particularly true in abortion and the handling of new-born calves or pigs

Third, a number of laboratory workers have developed the disease Huddleson<sup>13</sup> reports three cases among his confreres, and four scientists of the U S Public Health Service have contracted undulant fever

## CASE REPORT

The case to be reported is that of a telephone construction engineer, 30 years of age. The patient drank raw cow's milk habitually but used no goat's milk, and did not come in contact with domestic animals. He was referred to me after having been treated for two weeks, the provisional diagnosis being gripe and tuberculosis.

The symptoms were fever, sweating, nervousness, anorexia, afternoon headache, tremor, and cough.

The fever began so gradually that the patient continued to work for the first week. At the end of the second week the temperature reached  $102^{\circ}$  each afternoon, with a drop to  $100^{\circ}$  in the morning.

The physical examination was practically normal except for tremor of the fingers and tongue, sweating, fever and exaggerated reflexes.

Urinalysis was negative. Hemoglobin 74%, erythrocytes 5,550,000, leucocytes 6,150, polymorphonuclears 28%, lymphocytes 66%, large mononuclears 4%.

These findings seemed sufficient to exclude tuberculosis, typhoid fever, and rheumatic fever. Undulant fever was suspected, and an agglutination test requested. This was found positive, at about the 18th day of illness, in dilution of 1 to 320. Two weeks later it had increased in titer to 1 to 2,560 (*Brucella abortus*).

Two blood cultures and two urine cultures were negative.

The course of the fever was atypical. It subsided during the fourth week. For three days the temperature was normal. Then for one week only

fever recurred, reaching  $105^{\circ}$ . The administration of Mulford's Anti-melitensis serum may have hastened the decline. There has been no further recurrence in fifteen months. However, the serum agglutination has remained strongly positive.

The physical signs were also atypical. The spleen was not felt at any time. There was no adenopathy. No arthritis or orchitis occurred and no muscular pains.

## DISCUSSION

This is a case of undulant fever due to bovine *Brucella abortus* apparently contracted from drinking cow's milk. The patient resided in a city of over 150,000 inhabitants, where the milk is carefully inspected. However, no tests are made to determine the presence of *Brucella abortus* in the milk. Nor are the herds tested to determine the prevalence of infection.

The incidence of infection of cow's milk with *Brucella abortus* is surprisingly high. One authority estimates that at least 90% of our dairy herds are infected.<sup>14</sup> Presumably even certified milk from such herds would be contaminated. Pasteurization should destroy the organism.

An illuminating chapter in the epidemiology of *Brucella abortus* was recently written at the Metropolitan Life Insurance Company Sanatorium, at Mount McGregor, N. Y. Patients and staff men were tested for one year for *Brucella abortus*. Out of 599 sera, 82 gave a positive agglutination. Several infected cows were then removed from the company herd, and for eight months no new patients came down



with *Brucella* infection. However, after this interval, nine additional patients became infected, and a check-up of the herd showed that another animal had a positive agglutination.<sup>15</sup>

It would seem that we are facing a new public health problem inherent in the dairy and hog-raising industries. In the previous generation notable progress was made by Bruce, Hughes, and others, to control undulant fever due to goat's milk. In our generation Huddleson and Evans have pointed the way to safeguard our milk supply.

The problem is somewhat analogous

to that of bovine tuberculosis. The elimination of tuberculin-positive cattle is rapidly becoming an accomplished fact. For *Brucella* infection a similar campaign of elimination may be feasible.

The danger of transmission from animals to man undoubtedly is much greater than has been realized heretofore. Several fatal cases are already recorded and the morbidity is very great in many cases that recover. With current simplification of the diagnosis many more cases will probably be discovered.

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# Medicine And The Muse

Oliver Wendell Holmes, M.D.

By LILLIAN CONNOR LOUIS H. RODDIS, *Washington, D C*

GENTLEMEN DAMN the sphenoid bone! This was the annual preface to the lecture on the sphenoid given by Dr Holmes to freshmen medical students at Harvard during their course in osteology. As he was Parkman Professor of Anatomy from 1847 to 1882, a period of thirty-five years, it became a sort of ritual a kind of annual event at Harvard to which students looked forward. Every physician and student of medicine will know the reason for such profanity in reference to the sphenoid, for with the exception of the temporal bone it is the greatest stumbling block to the medical student in his whole course in osteology. Cunningham's Anatomy gives sixty separate facts it is necessary to learn about this small keystone of the skull. There are sixty-four descriptive facts given about the temporal bone and it is largely a matter of individual taste or rather distaste, as to which constitutes the worst obstacle to the student. The weight of medical tradition, however, indicates the sphenoid and Dr Holmes expressed the opinion of many a long-suffering freshman.

Oliver Wendell Holmes was born at Cambridge, Massachusetts, on the 29th of August, 1809. His father was the Reverend Abiel Holmes, a Calvinist

preacher. His mother, Sarah Wendell, was a descendant of Governor Simon Bradstreet, distinguished in the early history of the Massachusetts colony. He was at first destined for the law but soon began the study of medicine, a profession in which he was to take a high place as the co-discoverer with Semmelweiss of the method of transmission of puerperal sepsis and its prevention.

It was while a student at Harvard that Holmes leaped to fame as the author of some verses that have been repeated so frequently by American school boys that few productions of an American poet are more universally known. The Navy Department had decided to sell the old frigate Constitution celebrated for her victorious engagements with the British frigate Guerriere, and the sloops Cyane and Levant, as well as for her escape from the British squadron of Sir George Collier. There was much public disapproval of the sale but it was not sufficiently well expressed to deter the Navy Department from going ahead with its disposal. Then there appeared in the Boston Daily Advertiser the stirring lines of "Old Ironsides"

Aye, tear her battered ensign down!  
Long has it waved on high,  
And many an eye has danced to see



OLIVER WENDELL HOLMES, 1809-1894

That banner in the sky,  
Beneath it rung the battle's shout,  
And burst the cannon's roar,—  
The meteor of the ocean air  
Shall sweep the clouds no more!

This poem was reprinted everywhere and the wave of enthusiasm it caused so crystallized public sentiment that it led to the rescinding of the order to sell the old vessel

In 1833 young Holmes went to France to continue his medical studies. That country then held the place now occupied by Germany as a center of medical research and the names of Lous, Laennec, Broussais, Corvisart, Larrey, Dupuytren, and Velpeau gave the prestige to French medicine that in our day is conferred on Germany by those of Koch, Klebs, Löffler, Ehrlich, von Behring, Billroth, and von Esmarch.

In 1835 Holmes returned to Boston and began practice. During this period from 1835 to 1845 the valuable observations in reference to puerperal sepsis were made that form his principal contribution to medical progress and which give him a noteworthy place in the history of American medicine. Childbed fever was then like smallpox before vaccination a dreaded disease, the cause and mode of transmission of which were unknown.

In 1843 in the *New England Quarterly Journal of Medicine* Holmes published an article, "The Contagiousness of Puerperal Fever," and in it he boldly and plainly stated that puerperal sepsis was contagious and doctors and nurses the principal carriers of the infection. This statement was supported by the strongest sort of evi-

dence. He gave a careful summary of the observations that led to this conclusion. His recommendations for prevention were so simple and yet so correct that had they been adopted they would have at once resulted in a tremendous reduction in maternal mortality. The essay is rightly considered one of the classic documents in medical literature and should be read by every physician, not only because it contains the original announcement of an epoch-making observation that has led to the saving of millions of lives and the prevention of an enormous amount of human suffering, but as an example of clear and logical reasoning and of a fine yet restrained literary style. Not the least important part of Holmes' paper was the generous credit he gave to earlier students of the subject. This is particularly true of Charles White of Manchester to whose pioneer work he makes frequent reference. The bibliography at the end of the article also furnished a very complete review of the literature of puerperal fever.

Holmes met with the most bitter opposition from the leading obstetricians of the day and the weight of their influence effectually prevented any general adoption into practice of his views. However, in 1847 Semmelweis announced from the clinic of the *Allgemeines Krankenhaus* in Vienna that puerperal sepsis was due to absorption into the blood from the genitals of decomposed animal matter and that the hands or any article brought into contact with the genitals of the parturient, might be carriers of the contagion. By simple measures he reduced the mortality of the lying-in-wards of the

Krankenhaus from 114 per cent to 127 per cent. It is of interest to compare the recommendations of Holmes and Semmelweiss

Both Holmes and Semmelweiss were directed to the inquiry of the subject by similar circumstances. Holmes was struck by the frequency of post mor-

#### HOLMES

- 1 A physician holding himself in readiness to attend cases of midwifery should never take any active part in the post mortem examination of puerperal fever cases
- 2 A physician present at such post mortems should use thorough ablution, change every article of dress, and allow twenty-four hours or more to elapse before attending a case of midwifery
- 3 Similar precautions should be taken after the autopsy or surgical treatment of cases of erysipelas if the doctor is obliged to unite such duties with his obstetrical work, which is in the highest degree inexpedient

#### SEMMELOWEISS

- 1 Thorough washing of the hands with soap and hot water
- 2 Cleaning of the finger nails
- 3 Immersing the hands into a solution of chlorin water (later he recommended a chlorid of lime solution)

tem sepsis in the practice of physicians after they had been performing autopsies. Semmelweiss was present at the autopsy performed on his friend and demonstrator of anatomy, Professor Kolletschka, who died from an infection following the pricking of his finger while performing a post mortem. He observed the similarity of the finding in Kolletschka's body and in those of women who had died of puerperal fever. Semmelweiss met with opposition of a more violent character even than had Holmes and the remainder of his life was devoted to controversy and struggles for the general adoption of the methods of prevention he had put into practice at the Vienna Allgemeines Krankenhaus. The fight was a long and bitter one and ended only with the death of Semmelweiss and though he did not receive recognition during his life time he was scarcely dead when his work was accepted and with the advent of Lister, Pasteur, and Koch its true worth was revealed.

Semmelweiss deservedly holds the

highest place in the history of the conquest of childbed fever, but Holmes will not be forgotten as the greatest of the pioneers in the field, for the generous credit he gave to previous workers, and the classic excellence of the essay in which his results were given to the world. Both Holmes and Semmelweiss possessed the high moral courage required of the heretic and the rebel in stating their convictions. Child-bearing women of every land and time owe a great debt of gratitude to both of these men, and womanhood everywhere would honor itself with tributes to their memories.

In 1856 Holmes began the publication in a series of essays under the title of the "Autocrat of the Breakfast Table." Their success was such that the Professor at the Breakfast Table and the Poet at the Breakfast Table followed. From the beginning of the Autocrat, Holmes devoted himself more and more to literature and soon gave up the active practice of medicine. He was however in 1847 ap-

pointed Parkman Professor of Anatomy at Harvard and his work there kept him in close contact with his profession. His lectures were looked upon by the students as oases in an educational desert and this despite the fact that anatomy is commonly regarded as a rather dry subject. As seen by the opening sentence to his lecture on the sphenoid bone, his methods of instruction were such as to command attention. It is said that his classes were held toward the close of the day as he was the professor who could best hold the interest of tired students. Whether this was true or not, his lectures were long remembered with pleasure by those who attended them and many are the anecdotes recorded and unrecorded of the lecturer and his instructions.

Holmes fame as an essayist was established by the Autocrat, but it is not so well known that his medical essays are of equally high quality and that most of them may be read with pleasure by the laymen as well as the physician. In addition to the essay on puerperal fever which was reprinted by him in 1855 they include a delightful essay on Homeopathy and its Kindred Delusions, Border Lines of Knowledge in some Provinces of Medical Science, Currents and Counter Currents in Medical Science, Scholastic and Bedside Teaching, The Young Practitioner and Medical Libraries. Two essays, The Medical Profession in Massachusetts, and Some of My Early Teachers, are valuable contributions to medical history. A little known though interesting sketch is a lengthy introduction by Holmes to a little book called Visions,

A Study of False Sight (Pseudopia) by E. H. Clarke, published in Boston in 1878.

The humor that distinguishes the essays is found throughout the poetry. The verses telling of the effect of this humor on a servant is a characteristic piece of writing.

He took the paper, and I watched,  
And saw him peep within  
At the first line he read, his face  
Was all upon the grin

He read the next, the grin grew broad,  
And shot from ear to ear,  
He read the third, a chuckling noise  
I now began to hear

The fourth, he broke into a roar,  
The fifth his waist band split,  
The sixth, he burst five buttons off,  
And tumbled in a fit

Ten days and nights, with sleepless eye,  
I watched that wretched man,  
And since, I never dare to write  
As funny as I can

Holmes was in great demand at class reunions, alumni association dinners, at the entertainment of visiting notables and indeed all sorts of public social affairs. His invariable contribution was a poem and some of his happiest efforts were for these occasions. This stanza for a Harvard alumni reunion in 1857 is an example.

What dreams we've had of deathless name,  
As scholars, statesmen, bards,  
While Fame, the lady with the trump, held  
up

His picture cards!  
Till, having nearly played our game, she  
gayly

Whispered, Ah!  
I said you should be something grand,—  
You'll soon be grandpapa

More serious, yet in a playful mood too, is "The Boys" for the Harvard reunion of 1859. The gray haired men gathered there preserve the illusion that they are still the youngsters of the old days on Harvard's famous campus.

We've a trick, we young fellows, you may  
have been told,  
Of talking (in public) as if we were old  
That boy we call "Doctor", and this we  
call "Judge",  
It's a neat little fiction,—of course it's all  
fudge  
That fellow's the "Speaker"—the one on  
the right,  
"Mr Mayor", my young one, how are you  
tonight?  
That's our "Member of Congress", we say  
when we chaff,  
That's the "Reverend" what's his name?—  
don't make me laugh

And the fine concluding lines

Then here's to our boyhood, its gold and  
its gray!  
The stars of its winter, the dews of its  
May!  
And when we have done with our life-  
lasting toys  
Dear Father, take care of thy children,  
THE BOYS!

Here are the opening lines to verses read at what must have been a more convivial dinner, that given for Admiral Farragut July 6, 1865.

Now, smiling friends and shipmates all,  
Since half our battle's won,  
A broadside for our admiral!  
Load every crystal gun!  
Stand ready till I give the word,—  
You won't have time to tire,—  
And when that glorious name is heard,  
Then hurrah! hurrah! and fire!

His fame as a poet, of course, does

not rest on this relatively light and fugitive verse but on such splendid pieces as *Old Ironsides*, *The Battle of Bunker Hill*, *The Wonderful One Hoss Shay* and the *Chambered Nautilus*, the latter one of the best known and most widely quoted poems in the English language.

Dr Holmes wrote the most extensive collection of what may be called "medical poems" in the language. There are more than twenty devoted to themes in which only a physician would show interest and containing the medical terms suitable to the subject. There are *The Stethoscope Song*, *Extracts from a Medical Poem*, *Rip Van Winkle, M.D.*, *Meeting of the National Sanitary Commission* and verses on *Joseph Warren, M.D.*, the physician patriot whose death at Bunker Hill was so great a loss to the cause of the colonists. There is a poem in honor of Keats, also a physician, and a fine eulogy to the medical profession is contained in verses read at the Centennial Anniversary Dinner of the Massachusetts Medical Society June 8, 1881. There are some unmistakable expressions in the *One Hoss Shay* that inform us that the author was a doctor.

Many physicians have abandoned medicine for letters and as Sir William Osler has pointed out, many physicians have attained fame as men of letters but they have done so at the expense of opportunities for distinction in their profession. Holmes is the only exception. In him we have one who was famous in both fields, medicine and literature, and in the latter a master of two mediums, poetry and prose.

Dr. Holmes was a notable member of the famous Saturday Club of Boston where Longfellow, Whittier, Emerson, Lowell, Sumner, Motley, Parkman and Agassiz were accustomed to gather. Among them all he was regarded as the best conversationalist. He talked even better than he wrote. Throughout his long and active life he was a leading figure in Boston's social literary and professional circles. He took no part in politics though he was an ardent abolitionist. His eldest son, now a member of the United States Supreme Court, served as an officer in the Union Army.

In 1886 he made a journey of four months in Europe where he was received everywhere with pleasure and respect. The degree of Doctor of Letters was conferred upon him by Cam-

bridge University, Oxford made him a Doctor of Civil Law, and Edinburgh University a Doctor of Laws.

After his return he wrote "One Hundred Days in Europe" in which he reviews the kindness, the hospitality and the praise he received there. In 1888 appeared the series of charming papers known as "Over the Teacups" and in 1889 the poem for his Harvard class reunion, "After the Curfew," distinguished for its pathos and its expression of noble hope. These three productions are remarkable as the work of a man of four score years, and show what accomplishments are still possible to a serene and splendid old age.

Dr. Holmes died October 7, 1894, and is buried in Mount Auburn Cemetery.

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## Editorials

### *THE MINNEAPOLIS CLINICAL WEEK*

Another year has come around, and the necessary plans are now being made for the Annual Clinical Meeting of the College, which is to be held this year in Minneapolis during the week of February tenth. The Minneapolis men have chosen this season, the coldest of their Winter, in order to demonstrate how comfortable they can make it for their visitors. They promise a clear, dry, cold atmosphere, sparkling snow and brilliant sunshine, with Winter sports in great variety as external attractions, while internally there will be perfectly heated and ventilated rooms, with that degree of comfort which only the inhabitants of the Northwest know how to provide against the rigors of their climate. Long experience has perfected in them the art of adapting life perfectly to their long and cold Winters, and the visitor from warmer climates may be assured that this clinical session will be carried out under conditions even more comfortable than would be the case in warmer climes where the art and science of living warmly are less well developed. The attractions of Minneapolis as a city are many and varied, and it will be especially interesting to see it in the depth of its Winter season. The location of the twin cities upon the banks of the winding precipitous gorge of the Missis-

sippi, the frozen river, lakes and waterfalls, bordered by snowy forests, all offer a scenic setting of the greatest interest. The imagination is intrigued by the fact that the two cities of Minneapolis and St. Paul, so closely connected as to seem but one, are in reality the Gateway to the Great Northwest, the land of wheat, the endless plain of Minnesota and the Dakotas, stretching illimitably into Manitoba and the frozen North. When one stops to think of the youth of the land, barely a generation from the Indian, the immigrant wagon and the homesteader, amazement must fill the mind at the wonderful growth and development of this region in the last fifty years. The giant grain elevators and flour mills speak eloquently of the chief causes of that development, and the source of the wealth so evident in the buildings and homes of the two cities. The University and the Art Galleries of Minneapolis speak also for the development of intellectual culture which has paralleled that of the material prosperity of the city. And its medical development has been as amazing, as one will see from the article and illustrations by Dr. Marx White in this issue, in which are described and shown the numerous capacious and up-to-date hospitals of the community. To these medical facilities furnished by various social factors and agencies the University Medical

School must be the pivotal center around which all revolve, and from which all receive helpful stimuli. Here in the school and in the outlying hospitals and clinics a wonderful postgraduate week of clinical instruction and demonstration is being arranged for the Clinical Week. It is hoped that this wonderful opportunity, which is prepared for the Fellows and Associates of the College, will be made use of by a goodly representation, and that this meeting will pass into the history of the College as one of its best and largest. Therefore, each Fellow and Associate is urged to plan now to come to Minneapolis in February. A break in professional work in this month is highly desirable, an instructive vacation of a week in postgraduate work cannot fail to be most highly stimulating and profitable, and he who attends will go back to his work freshened in mind and spirit, and with a new zest. Not the least of all the advantages of Clinical Week is the opportunity it offers for the renewing of social relations among the members of the College. This after all is one of the chief functions of the annual meeting. The College is acquiring a distinguished personnel in its membership—it is good for these members to come together, to know one another personally and to establish bonds of intimacy and friendship. Through such the ideals of internal medicine for which the College stands can be brought closer to realization.

### *SENSATIONAL SCIENCE*

The recent widely heralded alleged discovery in the public press of the etiological agent of influenza leaves an

unpleasant taste in one's mouth. In the first place the manner of announcement discredits the achievement, whatever that may be. The proper place for the report of such a discovery is through the pages of a scientific journal, or through the medium of a scientific society directly interested in the branch of science concerned. But when an alleged scientific discovery is given out through the columns of a daily paper, then, at once, one is justly suspicious that desire for public notoriety, rather than scientific zeal, lies at the bottom of the announcement. Modern sensational journalism has invaded the sacred precincts of the investigating laboratory. Medical research of a certain kind has taken on a news value, and the reporter haunts the doors of science as he does those of the police station or of Congress. He applies the same criteria of sensationalism to the material he selects for publication from all of these sources. What has public interest is only that which will cause a cheaply sensational momentary thrill of interest in the minds of the readers, the majority of whom read only the head-lines. In the truly scientific accomplishment the journalist has no interest, and scores of splendid contributions to medical knowledge are passed unnoticed, because they lack such news value. But a cancer cure, a cause for cancer, the cause of influenza, and the like, offer possibilities for tickling the fleeting interest of the average reader, and hence have what is popularly called a news value. Wholly regardless of the futile hopes exalted in the breasts of thousands of cancer victims the newspapers will callously publish, almost from

day to day, accounts of the discovery of new cancer cures, which soon pass into oblivion and are forgotten by all except the friends of the victims whose hopes were so cruelly excited only to be blasted. The newspaper records of the International Congress of Physiology, held in Boston last August, are very revealing. Take the leading New York dailies, for instance, they suffer from the very same type of journalism. Of all the worthy and truly scientific matter presented at that Congress there was practically no notice taken, but columns appeared relating to various pseudoscientific accounts of cancer and rejuvenation presented at the meetings. In this respect the papers assume the value of a fake teacher and a false prophet in the choice and dissemination of such news material. The worst aspect of the whole situation is its reaction upon certain scientific men and research institutions, they actually came to encourage the premature publication of scientific investigations, or to give to their work an assumed importance which scientifically it does not possess. Even a suspicion of intentional dishonesty attaches itself to some newspaper performances of this kind. If not that, certainly the poorest possible judgment and questionable taste. In a popular journal devoted to the home there appeared recently a sensational article on Undulant Fever stating that thousands of cases of this disease were due to milk drinking, when as a matter of fact the Public Health Reports list less than a thousand cases all together. Not always, however, is the scientist, himself, to blame for the sit-

uation in which he may find himself. The reporter may twist and exaggerate, select words or phrases without context, and give to the reader an entirely wrong conception of an honest piece of work. Even with the greatest care an honest and modest worker may be caught. The attempt to control the situation by the development of special news agencies, such as Science Service, is subject to the same criticism, because of the choice of news exercised, the same false conception of material used. The harmfulness of the situation can be easily seen if one looks back through the daily papers of the last ten years and notes the so-called great medical discoveries that have held first place, with headlines, in their columns. Where are they now, these great discoveries? Where is the Gye-Barnard cause of cancer, the cancer bacillus, the Blair Bell lead treatment, the Noguchi cause of Yellow Fever, the Voronoff and Steinach methods of rejuvenation, and a dozen others? In the same limbo to which will be presently consigned the Gerson diet-cure for tuberculosis, the Calmette method of immunization, the Pearl treatment of cancer with tuberculin, and, most probably, the recent discovery of the cause of influenza. It is unfortunate that the public interest in medical matters cannot be more intelligently directed, so that medical discoveries will be accorded their real value, and no false hopes excited. Surely there are definite moral principles involved in this giving out and the publication of the results of medical research.

## Abstracts

*A Study of the Pellagra-Preventive Action of Canned Salmon* By JOSEPH GOLDBERGER and G A WHEELER (Public Health Reports, Nov 15, 1929)

A test of the black tongue-preventive action in the dog of canned salmon showed that it had a decided preventive action, resulting in full protection against this condition. In view of the abundant evidence that canine black tongue is the analogue of human pellagra, a comparable study of the value of canned salmon in pellagra was organized at the Georgia State Sanitarium, in Milledgeville, in 1927. The results of this study are reported here. Canned Alaska chum salmon was used. The entire contents of the can, including bone, skin and liquid portion, were thoroughly mixed and incorporated in the cooked cereal-legume portion of the basic diet. Each patient was allowed six ounces of salmon per day, receiving approximately 17 ounces with the morning and evening meals, and 26 ounces at midday. A total calory diet of 2,050 was given daily. The basic articles of diet were cornmeal, cowpeas, wheat flour, lard and tomato juice. Cod-liver oil and calcium carbonate were also given. A total of 18 white female patients came under observation for pellagra-preventive treatment with this diet during the period of the test, all of whom remained under continuous observation for a period of not less than one year. None of these presented, at any time, any symptoms of pellagra. In the light of repeated experience it seems safe to state that, without the salmon or some other equivalent preventive, in the diet, not less than 40-50 per cent of them would have suffered a recurrence within a period of from three to seven months. The fact that none of the group showed symptoms even suggestive of pellagra would seem to be convincing evidence of the pellagra-preventive action of the salmon and of the pel-

lagra-preventive factor in canned Alaska chum salmon. The quantity of salmon allowed was fairly liberal. Whether a smaller allowance would have been equally effective cannot be stated. The demonstration that salmon contains the pellagra-preventive factor is of considerable interest. In the first place it is a readily available preserved food, comparatively cheap, and if used in sufficient quantity, constitutes a dependable substitute for fresh meat, at least in so far as the pellagra-preventive factor is concerned. The results are also in harmony with certain previously recorded experiments showing that substances possessing black-tongue preventive potency are also preventives of pellagra, and thus furnish additional evidence that black tongue in dogs is the analogue of pellagra in man. By reason of its potency in the P-P factor, and its availability, salmon may be considered a fair substitute for meat in the areas of pellagra endemicity when meat is not readily available.

*Vitamin D in Tuberculosis* By B KRAMER, H G GRAYZEL, and M J SHEAR (Proc Soc f Exper Biol and Med, November, 1929, p 144)

During studies made by these workers in 1926 the question rose repeatedly as to whether vitamins play an important rôle in the etiology and treatment of tuberculosis. Ultra-violet light has in recent years been found of value in the treatment of intestinal tuberculosis, heliotherapy has been used with success in other forms of tuberculosis, calcification is often found in healed tuberculous lesions. These considerations suggested a possible linkage between tuberculosis and the vitamin D content of the diet. In the older literature, cod liver oil is mentioned as of value in the treatment of tuberculosis. This beneficial result, sometimes obtained, may not have been due to the fat

but to the vitamins present in the oil. In the present study irradiated cholesterol, cod liver oil concentrate and irradiated dried yeast powder were employed. Subsequently, biologically assayed cod liver oil was added to the number of preparations studied. Eighteen tuberculous children were divided into 2 groups of 9 each, one was the test group, the other the control. One child had tuberculosis of the skin, the others had active bone tuberculosis. All received a well-balanced diet. The treated children received daily 4 mg irradiated ergosterol (Fleischman) during the first 4 months and 7 mg for the succeeding 8 months (0.0001 mg of the irradiated ergosterol per rat per day produced a continuous line in rachitic rats in 7 days). Physical examinations of the children were made periodically, as well as blood pressure readings, urine analyses, roentgenograms and analyses for serum calcium and phosphorus. The results were summarized, as follows. The daily addition of a large amount of vitamin D did not produce any detectable acceleration of the healing process. Such doses of irradiated ergosterol produced no discernible deleterious effects. The administration of irradiated ergosterol for 12 months produced no increase in either serum calcium or phosphorus.

*The Effect of Restricted Diet and Suprarenalectomy on Experimental Tuberculosis in the White Rat* By MAXIM STEINBACH (Proc Soc f Exper Biol and Med, November, 1929, page 142)

It has been previously demonstrated that the albino rat enjoys complete immunity to infection by human tubercle bacilli in spite of the fact that the bacteria remain alive for indefinite periods and apparently multiply in the host. In the first series of experiment described 36 rats were used and divided into 3 groups. 12 were inoculated with human, 12 with bovine and 12 with avian strains of the tubercle bacillus. All strains used were pathogenic. 6 of each of these groups were on a bread and water diet, and 6 on a full maintenance diet. Those on the restricted diet given the human and bovine strains showed no macroscopic or micro-

scopic evidence of tissue reaction. In smears and tissue stains many of these animals showed the presence of the tubercle bacillus. 82 per cent of those inoculated with the avian strain showed extensive macroscopic lesions. The control groups were negative as to human and bovine infection, but with the avian strain 50 per cent were found at autopsy to have extensive tuberculous lesions. From these experiments it was concluded that the white rat is immune to the human and bovine strains of the tubercle bacillus, even when its resistance is lowered by a deficient diet, but is susceptible to the avian strain. It was noted, however, that a greater percentage of infections took place among those fed on a restricted diet than among those normally fed. On the basis of these conclusions it was decided to investigate the possibility of infection with the bovine as well as the avian strain in animals whose resistance is lowered by bilateral suprarenalectomy. A large number of animals were suprarenalectomized, and were subsequently inoculated on the fifth day postoperative with either bovine or avian tubercle bacilli. Most of the animals died soon after. Of those that lived, 16 had been inoculated with the bovine organism and 5 with the avian. Of the 16 animals in the bovine group, 12 survived for periods ranging from 7-22 days. Of these 12, all but one showed definite macroscopic or microscopic (or both) evidence of tubercle formation and tubercle bacilli were demonstrated in the tissues. The remaining 4 in this group were killed; three of them showed definite macroscopic lesions. In the fourth, no lesions could be found. Therefore, of the 16 animals, all but 2 showed definite evidence of tubercle formation as the result of infection with the bovine strain of tubercle bacilli. Of the 5 suprarenalectomized animals inoculated with the avian bacilli, all were found at autopsy to have extensive tuberculous lesions. In the previous experiment it was shown that only 50 per cent of normal rats inoculated with the avian strain developed characteristic tuberculous lesions. In the previous experiment it was shown that only 50 per cent of normal rats inoculated with the avian

strain developed characteristic tuberculous lesions. It was, therefore, deemed unnecessary to use additional controls for this group. It appears then that bilateral supra-renalectomy in the albino rat lowers the resistance so that subsequent inoculation with the bovine tubercle bacillus results in

definite tissue reaction, with tubercle formation and caseation, resembling human tuberculosis. This does not occur in normal rats or in rats on a restricted diet. Suprarenalectomy, and to a less extent, deficient diet, increase the susceptibility of albino rats to the avian tubercle bacillus.

## Reviews

*Pathogenic Microorganisms* A Practical Manual for Students, Physicians and Health Officers By WILLIAM HALLOCK PARK, M.D., Professor of Bacteriology and Hygiene, University and Bellevue Hospital Medical College and Director of the Bureau of Laboratories of the Department of Health, New York City, and ANNA WESSELS WILLIAMS, M.D., Assistant Director of the Bureau of Laboratories of the Department of Health, and CHARLES KRUMWIEDE, M.D., Assistant Director of the Bureau of Laboratories, Associate Professor of Bacteriology and Hygiene in the University and Bellevue Hospital Medical College, New York City Ninth Edition, Enlarged and Thoroughly Revised 819 pages, 216 engravings and 9 full-page plates Lea and Febiger, Philadelphia, 1929 Price in cloth, \$6.50 net

The first edition of this book was called *Bacteriology in Medicine and Surgery*, and was written to make available for others the practical knowledge acquired in the bacteriological laboratories of the city of New York, and was intended more for medical practitioners than for medical students or laboratory workers. In the third edition the study of the pathogenic protozoa was included, and the title broadened to include the whole field of pathogenic microorganisms. At the same time the subjects were treated in a more comprehensive manner, so as to make it a suitable textbook for medical students. In the fifth edition the material was rearranged in order to bring together more closely all of the pathogenic microorganisms. In the eighth edition further rearrangements were made so that the grouping of different microorganisms conformed more closely to the classification adopted by the Society of American Bacteriologists. The new terminology was added to the older common names and sev-

eral new comprehensive tabulations were given. In the present edition the many additions to our knowledge during the past three years have necessitated a very extensive revision, and many parts of the book have been completely rewritten. The sections on immunity have been amplified, particularly with reference to the experience of the authors with active immunization against diphtheria and scarlet fever. The chapters on the pyogenic cocci, paratyphoid bacilli and pneumococci have been practically rewritten. The recent additions to our knowledge of scarlet fever, measles, yellow fever, undulant fever and tularemia have been accorded due attention. Numerous other changes and additions bring this work quite up to date, and the result is a very complete and reliable textbook, well illustrated, and one thoroughly to be recommended. That it has reached its ninth edition is sufficient proof of its excellence.

*Selected Readings in Pathology* From Hippocrates to Virchow Edited by EDMOND R. LONG, Professor of Pathology, University of Chicago. 301 pages, 25 plate illustrations Charles C. Thomas, Springfield, Illinois—Baltimore, Maryland. Price in cloth, \$4.00

This volume consists of a series of excerpts from the classics of pathology, republished in the wish to lay before physicians and medical students some of the original documents in the evolution of this fundamental branch of medical science. The works from which they are taken are constantly quoted in the class-room in pathology, but being more or less inaccessible are not often read by the student. The book does not pretend to present a connected view of the evolution of pathology, but simply to furnish, in a frankly, discontinuous way, a more intimate acquaintance with some of the greater masters of the science. Some

of the extracts are of especial historical significance as marking mile-stones in our progress in the knowledge of disease, others are representative samples of certain lengthy volumes which were of unusual influence. There are thirty-six masters represented, from Hippocrates to Virchow, including a number of less familiar names. The book serves a very useful purpose, and is to be recommended to medical students, for additional reading in courses of medical history.

*Hookworm Disease Its Distribution, Biology, Epidemiology, Pathology, Treatment and Control* By ASA C CHANDLER, M Sc, Ph D, Professor of Biology, Rice Institute, Houston, Texas, Recently Officer-in-Charge, Hookworm Research Laboratory, School of Tropical Medicine and Hygiene, Calcutta, India. 494 pages, 33 figures. The MacMillan Company, New York, 1929. Price in cloth, \$5.00.

Hookworm infestations are engaging the attention of the medical profession and of governments in every tropical and subtropical country in the world to a greater extent than ever before. There is probably no important and widespread human disease in which so many important and diversified contributions to knowledge have been made within the last decade, as has been the case with hookworm disease. All phases of the subject—geographic distribution, biology, epidemiology, pathology, diagnosis, treatment or control—have received attention from numerous skilled workers during this time with important results. Much of the recent work on hookworm has been made possible by the development of new research methods. Because of the great economic importance of the subject, of the great recrudescence of interest in it, and the lack of any adequate comprehensive modern account of it, the writer has attempted to bring together the work of recent years and to coordinate it with older work, in order to make it available in a convenient form for research workers, medical men and sanitarians in the many parts of the world where no such comprehensive knowledge is available in any form. This book

contains a wealth of facts of greatest importance to mankind, in its relationship to problems of public health and practical medicine. It is an indispensable work to those interested in this subject. The book is well printed, and the illustrations are satisfactory.

*Modern Methods of Treatment* By LOGAN CLENDENING, M D, Professor of Clinical Medicine, Lecturer on Therapeutics, Medical Department of the University of Kansas. With Chapters on Special Subjects by H C ANDERSON, M D, J B COWHERD, M D, and others. Third Edition. 815 pages, 95 illustrations. C V Mosby and Company, St Louis, 1929. Price in cloth, \$10.00.

This third edition follows close upon the heels of the second. It has been carefully revised. The account of diathermy has been rewritten. The articles on quinidine sulphate, liver in anemia and iodine in goiter have been revised. The account of non-specific protein therapy has been amplified, particularly as to its application to peripheral vascular disease. Synthaline, myrtilin, euphyllin, sulphocyanate, barium chloride and erysipelas antitoxin have received brief mention. The author has not endeavored to add every suggested change in therapy that has developed since the last edition, but his inclusions have been conditioned by his experience and judgment as to what methods are firmly established and supported by scientific evidence. The general plan and purpose of the book remain unchanged. This edition shows great improvement over the preceding in many sections. Others remain too superficially treated. Some discussions are excellent and notable for their common sense view.

*Hemorrhoids The Injection Treatment and Pruritus Ani* By LAURENCE GOLDBACHER, M D. 205 pages, 31 half-tones and line engravings, some in colors. F A Davis Company, Philadelphia, 1930. Price in cloth, \$3.50.

The purpose of this book is to present to the medical profession practical and readable information concerning hemorrhoids and pruritus ani, in as simple and brief form as



possible. A portion of the material has already been published in various medical journals, and with slight changes is here presented with the hope that it will stimulate further investigation. Hemorrhoids constitute the most frequent form of rectal disease, and are present in more than 50 per cent of patients afflicted with rectal ailments. During the World War there were 29,176 hospital admissions for hemorrhoids in the U S Army from April 1, 1917, to December 31, 1919, representing a total loss of 623,493 days. The actual prevalence of hemorrhoids in civil life cannot be estimated. They occur in all countries and climates and among all races, in all stations of life and in those of both sedentary

and active occupation. All cases of hemorrhoids are curable, and the majority without recourse to surgery. Because of the great amount of suffering and disability produced by them, their treatment demands the prompt and serious attention of the medical profession. The author employs the incision method for the treatment of external hemorrhoids, and the injection of phenolized oil for the treatment of internal hemorrhoids and pruritus ani. In his book the general considerations of these methods, with a description of the technique employed, are given in a clear and concise manner. It is well illustrated. It is recommended to those who are interested in this subject.

## College News Notes

Dr F M Pottenger (Fellow), Monrovia, Calif, addressed the St Louis Medical Society, October 29, on "The Relation of Symptoms of Disease to the Vegetative Nervous System" He also addressed the Columbus Academy of Medicine, November 4, on "Institutional Care of Tuberculosis"

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Dr C Lydon Harrell (Associate), Norfolk, Virginia, addressed the Tidewater Dental Association, October 17, on "Cooperation of the Physicians and Dentists" On October 23, he delivered a paper before the Virginia State Medical Society at Charlottesville, entitled "Thyroid Deficiency—A Clinical Study"

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Dr Bernard L Wyatt (Fellow), Tucson, Ariz, during October completed the incorporation of "The Wyatt Clinic"

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Dr George Morris Piersol (Fellow and Secretary-General), Philadelphia, Pa, spoke on "The Medical Society as a Teaching Institution", on November 1 at the first of a series of Postgraduate Seminars under the auspices of the Philadelphia County Medical Society

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Dr G Harlan Wells (Fellow), Physician-in-chief, Hahnemann Hospital, Philadelphia, recently described in detail "The Differential Diagnosis of Anemia", in a Medical Clinic at the Hahnemann Medical College

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The following Fellows of the College are among the speakers for the Postgraduate Seminars under the auspices of the Philadelphia County Medical Society

Dr Martin E Rehfuess (Fellow), "How frequently is Dyspnea a matter of Simple Dietary Perversion?"

Dr S Calvin Smith (Fellow), "Sudden Heart Failure"

Dr H R M Landis (Fellow), "Non-Tuberculosis Lung Lesions of Upper Lobe"

Dr E J C Beardsley (Fellow and Governor), "Clinical Demonstration of Chest Examinations"

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Dr Franklin H Martin, Director-General of the American College of Surgeons, advises that "In behalf of the officers and Regents of the American College of Surgeons, may I take this early opportunity to advise you that the next annual Clinical Congress of the College is to be held in Philadelphia, Pa, October 13-17, 1930"

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The 59th Annual Meeting of the American Public Health Association will be held in Fort Worth, Texas, during the week of October 27, 1930, with the Hotel Texas as headquarters Mr Homer N Calver, 370 Seventh Avenue, New York City, is the Executive Secretary

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The following members of the College are scheduled to speak at the "Health Talks" for the public under the auspices of the Philadelphia County Medical Society

Dr James M Anders (Master), "Where is the Layman Remiss in the Care of his Health?"

Dr William Devitt (Fellow), of Devitt's Camp, Allenwood, Pa, "Diet and Dissipation and Tuberculosis"

Dr George E Pfahler (Fellow), Cancer—the Prevention of its Increase"

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Dr Carl V Vischer (Fellow), Philadelphia, is co-author with Dr Edwin O Geckler and Dr Grant O Favorite of a "Report of Arthritis Conference, Hahnemann Hospital" This report was read at the meeting of the Homeopathic Medical Society of the State of Pennsylvania and was published in the November number of the Hahnemann Monthly

The following Fellows of the College were elected Officers of the Homeopathic Medical Society of the State of Pennsylvania

1st Vice President—Dr Henry I Klopp, Allentown, Pa

Secretary—Dr E Roland Snader, Philadelphia, Pa

Dr Lewellys F Barker (Fellow), Baltimore, Md, succeeds Dr Ray Lyman Wilbur as Chairman of the Medical Council of the U S Veterans' Bureau

Dr Emanuel Libman (Fellow), New York, addressed the Pittsburgh Medical Forum, October 26, on "Observations on Angina Pectoris of Various Origins"

Dr David C Hall (Fellow), Seattle, upon invitation of the Pan-Pacific Surgical Conference, issued by the Pan-Pacific Union, read a paper upon the medical aspects of Goiter in relation to surgery. The Conference was held in Honolulu, T H, during August. Nearly two hundred surgeons from all countries bordering the Pacific were in attendance

Dr George B Lake (Associate), Chicago, spoke, under the auspices of the Illinois State Medical Society, before the Parent-Teacher Association of Waukegan, Ill, on November 19, and before the University Club at Peoria, Ill, on November 26, his subject being, "Psychic Diseases and a Philosophy of Life"

The following Fellows of the College are members of the National Board of Medical Examiners of the United States

Walter L. Bierring, Des Moines, Iowa

Lewis A Conner, New York, N Y

Hugh S Cumming, Washington, D C

R D Harden, Washington, D C

M W Ireland, Washington, D C

Howard T Karsner, Cleveland, Ohio

W S Leathers, Nashville, Tenn

George W McCoy, Washington, D C.

C. E. Riggs, Washington, D C

Dr Walter L. Bierring is now President

Dr Harold Swanberg (Fellow), Quincy, Ill, addressed the annual meeting of the Northeast Missouri Dental Society at Hannibal, October 21, on "The Role of the Maxillary Sinus in General Infections"

Dr William M James (Fellow) of the Herrick Clinic, Panama, R P, has been invited by the University of London to deliver a course of six lectures on Tropical Medicine during 1930

Dr Lyell C Kinney (Fellow), San Diego, Calif, at the annual meeting held recently in Coronado, was elected President-Elect of the California Medical Association

Dr Benjamin Hobson Frayser (Fellow), Fort Harrison, Mont, was recently elected Surgeon-General of the national organization of the American War Veterans. Dr Frayser has also been appointed District Deputy for the States of Wyoming, Idaho, and Montana, Theta Nu Epsilon Society

Dr Henry W Grote, Bloomington, Illinois, has been re-instated as an active Associate of the College

Dr Henry J John (Fellow), Cleveland, addressed the Tulsa (Okla) Academy of Medicine, November 18, on "Diabetes"

A portrait of the late Dr Arthur S Loevenhart (Fellow), has been hung in the Auditorium of the Memorial Institute of the Wisconsin General Hospital at Madison. Dr Loevenhart was formerly head of the Department of Pharmacology of the University of Wisconsin Medical School

Dr P P McCam (Fellow), Sanatorium, N C, has been elected President of the Southern Tuberculosis Conference

Dr L R DeBuys (Fellow), New Orleans, recently resigned as Professor of Pediatrics and head of that department of Tulane University School of Medicine, a post he has held for eight years. He is

succeeded by Dr Robert A Strong of Pass Christian, Mississippi.

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Dr Lawrason Brown (Fellow), Saranac Lake, will be one of the speakers at the Pan-American Medical Association meeting at Panama City, January 30-February 3

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Dr William Gerry Morgan (Fellow), President-Elect of the American Medical Association was the recipient of an honorary meeting and dinner held in Washington, December 11, by the Medical Society of the District of Columbia. Civic as well as medical leaders of the community were in attendance, and a program suitable for the occasion was rendered. Dr Frank Leech (Fellow), Washington, was the Chairman of the Committee on Arrangements

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Dr Howard M Jamieson (Fellow), Decatur, Ill, addressed the Illinois Medical Library Association, December 5, on "Some notes on Diagnosis of Carcinoma of the Blood Serum"

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Dr Cyrus C Sturgis (Fellow), Professor of Internal Medicine at the University of Michigan Medical School, spoke before the Wayne County Medical Society at Detroit, November 19, his subject being "Treatment of Pernicious Anemia with Special Reference to Some Newer Methods"

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Dr George C Hale (Fellow), Professor and Chief of the Department of Medicine of the University of Western Ontario, London, Canada, gave a diagnostic clinic before the Highland Park Physicians' Club, December 5

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Dr John D Wilson (Fellow), Scranton, Pa, is a member of the Board of Directors of the Pennsylvania unit of the National Association Against the Prohibition Amendment

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Dr Francis D Murphy (Fellow), Wauwatosa, Wis, recently addressed the Ke-

nosha County Medical Society on Chronic Glomerulonephritis

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Dr Andrew C Ivy (Fellow), Chicago, addressed the Milwaukee Academy of Medicine, October 22, on "The Mechanics of Digestion with Special Reference to Bile Flow"

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Dr David P Scott (Fellow), Lynchburg, Va, delivered an address on "Medical Treatment" before the South Piedmont, (Va) Medical Society on November 26

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Dr William A White (Fellow), Superintendent of St Elizabeth's Hospital, Washington, D C, reviewed the past twenty years of work of the mental hygiene movement and discussed the coming International Congress on Mental Hygiene to be held in Washington next May, at the dinner celebrating the twentieth anniversary of the movement held in New York, November 1

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Dr B M Riley (Fellow), Omaha, Nebr, is the author of a paper entitled "Two Types of Vascular Disturbances of the Extremities", appearing in the December issue of the Nebraska State Medical Journal

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Dr Solomon Strouse (Fellow), Chicago, addressed the Cincinnati College of Medicine, November 14, on "Obesity"

---

Dr Hugh A McGuigan (Fellow), Chicago, addressed the Medico-Historical Club of the University of Illinois College of Medicine, November 7, on "A Sabbatical Year in Europe", illustrated with lantern slides

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Dr Carl J Wiggers (Fellow), Cleveland, addressed the Chicago Medical Society, November 20, his title being "The Clinical Physiology of Aortic Insufficiency"

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Dr George G Ornstein (Fellow), is now Associate Clinical Professor of Medicine at the New York Postgraduate Medical School and Hospital

## OBITUARY

Dr Peter J Calvy (Fellow), Fond du Lac, Wisconsin, died during October, 1929, aged 55

Dr Calvy received his medical training at the Wisconsin College of Physicians and Surgeons, graduating in 1903. He had been a teacher of nervous and mental diseases of medical practice at the St Agnes Training School for Nurses for some years. He was a member of the Fond du Lac County Medical Society, the Wisconsin State Medical Association, a Fellow of the American Medical Association and a Fellow of the American College of Physicians since April, 1920.

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Dr Stillman Smith Ham (Fellow), Schenectady, N. Y., died at his home, 1503 Union Street, December 9, 1929, of an acute heart attack. He had been in apparent good health, and had been receiving patients up to a half hour before his sudden death.

Dr. Ham was born in Schenectady, February 23, 1878. He received his

PhB degree from Union College in 1899, and his medical degree from the Albany Medical College in 1902.

From 1904 to 1914, Dr Ham was physician to the Day Nursery Dispensary and to the Children's Home, both of Schenectady. From 1917 to 1927, he was physician to the Old Ladies Home. Since 1919 he had been attending physician to the Ellis Hospital, and clinical instructor at the same institution for medical students of the Albany Medical College since 1920. For many years he was chief medical examiner for the Metropolitan Life Insurance Company.

Dr Ham was a captain in the medical corps of the Army during the World War, serving at Camp Gordon, Atlanta, Ga.

He was a member of the Schenectady County Medical Society (President, 1919), the New York State Medical Society and the American Medical Association. He became a Fellow of the American College of Physicians on April 10, 1917, having been one of the very early members. Dr Ham was highly esteemed and respected by all who knew him.

## REPORT, COMMITTEE ON NOMINATIONS

The Committee on Nominations, appointed by the President in accordance with the provisions of the By-Laws, respectfully presents the following nominees for the line offices of the American College of Physicians for 1930-31

President	Sydney R Miller, Baltimore, Md
President-Elect	S Marx White, Minneapolis, Minn
1st Vice President	Aldred Scott Warthin, Ann Arbor, Mich.
2nd Vice President	Francis M Pottenger, Monrovia, Calif.
3rd Vice President	John A Lichty, Clifton Springs, N Y.

W Blair Stewart, Chairman  
 E B Bradley  
 James S McLester  
 James H Means  
 Charles F Martin

## LIFE MEMBERSHIP

Three years ago the Board of Regents, believing a sound financial foundation to be one of the best guarantees of insuring the stability and perpetuity of the American College of Physicians, provided for the building up of an Endowment Fund, "the principal of which shall be held intact and invested in securities approved by the Board of Regents, while the income shall be available for carrying out the purposes of the organization" (See By-Laws, Article VIII)

This Endowment Fund "shall consist of (1) all moneys received for LIFE MEMBERSHIP in the College, (2) such moneys as may be set aside by the Board of Regents from time to time from the funds of the College, and (3) such moneys as may be donated directly to the fund"

The then President and President-Elect, Dr Alfred Stengel and Dr Frank Smithies, respectively, set the precedent by immediately subscribing \$500.00 each to the Fund by becoming Life Members. Since that time, several more Fellows have subscribed to Life Membership, some by full payment and others by subscribing \$100.00 per year for four years, which together with the \$100.00 initial Fellowship fee paid at time of election will amount to \$500.00. Total payments already made amount to \$4,700.00. This fund is already invested in securities approved by the Board of Regents.

The following constitutes the present list of Life Members

Lewellys F Barker, Baltimore, Md  
 Oscar Berghausen, Cincinnati, Ohio  
 Robert Bernhard, New Orleans, La  
 Carl R Comstock, Saratoga Springs, N Y  
 Charles F Martin, Montreal, Que  
 Nels C Meling, Evanston, Ill  
 John G Ryan, Denver, Colo  
 Adolph Sachs, Omaha, Nebr  
 Frank Smithies, Chicago, Ill  
 Alfred Stengel, Philadelphia, Pa  
 Noxon Toomey, St Louis, Mo  
 M Lawrence Turner, Berwyn, Md  
 A H Waterman, Chicago, Ill  
 Bernard L Wyatt, Tucson, Ariz

Life Members pay no more dues for the balance of their lives, they receive the official journal, Annals of Internal Medicine, without further cost, they receive the Directory every time revised and re-published, as well as other publications the College may have from time to time, they receive an engraved Life Membership Card, admitting them to every meeting and entitling them to take part in all College activities, their names will be engrossed on the permanent scroll of Contributors to the College Endowment Fund, they will be helping to build up a fund which will eventually enable the College to carry out a larger and more active program in the field of Internal Medicine

Subscription Form

ENDOWMENT FUND

LIFE MEMBERSHIP

I hereby subscribe Five Hundred Dollars (\$500) to the Endowment Fund of the American College of Physicians, the amount to include the \$100 paid already by me as my Fellowship fee at time of Election I elect the option checked below for the payment of the balance, \$400

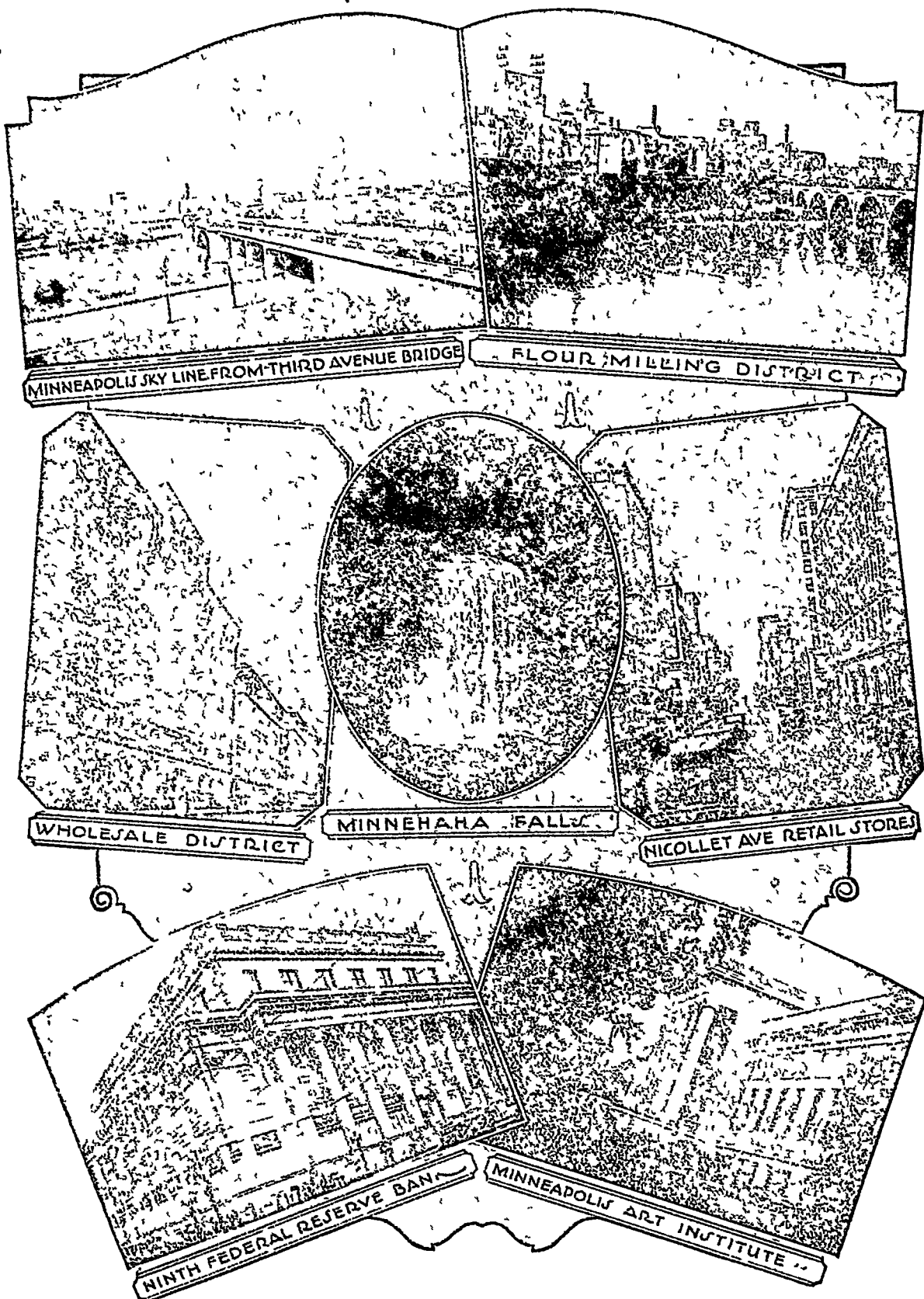
- A Payable in one lump sum during the present year
- B Payable in four annual installments of \$100 each, beginning . , 19

My annual dues shall cease at once if I elect Option A , or, if I elect Option B, when I have made three annual payments (\$300, total)

Upon full payment of this subscription, the sum of \$500 shall be credited to and become a part of the Permanent Endowment Fund of the College, and I shall become a LIFE MEMBER of the College

	Name	..
Date	Address	.

In case of death, all unpaid balances will be cancelled



MINNEAPOLIS SCENES  
 WHERE WE MEET — FEBRUARY 10-14, 1930  
 FOURTEENTH ANNUAL CLINICAL SESSION



## AMERICAN COLLEGE OF PHYSICIANS

Fourteenth Annual Clinical Session

Minneapolis, Minnesota

February 10-14, 1930

## MONDAY, FEBRUARY 10

Morning Registration  
 Afternoon Opening Session, which will include the addresses of Welcome and part of the Scientific Session  
 Evening Scientific Program

## TUESDAY, FEBRUARY 11

Morning Clinics  
 Afternoon Scientific Session  
 Evening Scientific Session

## WEDNESDAY, FEBRUARY 12

Morning Clinics  
 Afternoon Scientific Session  
 Evening Convocation, followed by Smoker

## THURSDAY, FEBRUARY 13

Morning Clinics  
 Afternoon Scientific Session, short, followed by General Business Meeting at 4 00  
 Evening Banquet

## FRIDAY, FEBRUARY 14

Morning Clinics  
 Afternoon Scientific Session

INDEX TO PLACE OF MEETING, CLINICS AND DEMONSTRATIONS  
 (Registration, Information, Scientific Sessions and Convocation at the Auditorium )

- A* University Hospitals  
Lecture Room, Todd Memorial Hospital
- B* University Hospitals  
Lecture Room, Eustis Memorial Hospital
- C* Institute of Anatomy, University of Minnesota.
- D* Veterinary Building, University Farm, St Paul
- E* Hennepin County Medical Society Assembly Room
- F* Minneapolis General Hospital  
Sun Porch.
- G* Minneapolis General Hospital  
Clinic Room
- H* St Mary's Hospital
- I* Swedish Hospital
- J* Abbott Hospital
- K* Northwestern Hospital
- L* Glen Lake Sanatorium

## AUDITORIUM

The place of meeting for the Opening Session Monday afternoon, Scientific Sessions Tuesday to Friday afternoons and Monday and Tuesday evenings, and for the Convocation, followed by the Smoker, Wednesday evening

Registration and Information Booths and the Commercial Exhibits are all comfortably housed on the same floor with the place of meeting, and ample provision is made for all the activities surrounding the Sessions

Grant Street between Stevens Avenue and Third Avenue South

## CLINICS AND DEMONSTRATIONS

- A-B* University Hospitals Ellott Memorial, Todd Memorial (Eye, Ear, Nose and Throat), Cancer Institute, Eustis Memorial (Pediatrics), Students' Health Service, together with the Out-Patient Department 400 beds
- A* Amphitheater, Todd Memorial Hospital  
Seating capacity 150
- B* Amphitheater, Eustis Memorial Hospital  
Seating capacity 150  
"Minneapolis-St Paul" streetcars, east-bound, on Fifth Street at Hennepin, Nicollet or Marquette Avenues (20 minutes) or bus, "St Paul via University Avenue" on Seventh Street at Hennepin, Nicollet or Marquette Avenues, or at Radisson Hotel (15 minutes)
- C* Institute of Anatomy, University of Minnesota Medical School Laboratories of Pathology, Anatomy and allied branches Auditorium seating capacity 226 Washington Avenue at Church Street, SE "Minneapolis-St Paul streetcars, east-bound, on Fifth Street at Hennepin, Nicollet or Marquette Avenues (20 minutes) or bus, "St Paul via University Avenue" on Seventh Street at Hennepin, Nicollet or Marquette Avenues, or at Radisson Hotel (15 minutes)
- D* Veterinary Building, University Farm  
Agricultural, Veterinary and Home Economics  
Departments of University of Minnesota  
St Anthony Park Seating capacity 125  
Como Avenue streetcar, east-bound, on Hennepin Avenue to Doswell Avenue  
Special bus for members of The College leaves Nicollet Hotel 7 45 A M, and takes on passengers at the Radisson, Dyckman, Curtis and Leamington Hotels
- E* Hennepin County Medical Society Assembly Room and Library Twentieth Floor of Medical Arts Building on Ninth Street South, between Nicollet and Marquette Avenues  
Seating capacity 350  
In Loop Walking distance from hotels
- F-G* Minneapolis General Hospital (Municipal) 689 Beds Entrance on Fifth Street South, between Sixth and Seventh Avenues
- F* Sun Porch, second floor Seating capacity 125
- G* Clinic Room, basement floor  
Seating capacity 70  
Chicago Avenue streetcar, south-bound, crosses Hennepin, Nicollet and Marquette Avenues at Eighth Street (10 minutes)

- H* St Mary's Hospital 2500 Sixth Street South  
General 350 beds (100 children)  
Seating capacity 400  
Seventh Street-Minnehaha-Hazel Park streetcar, south-bound, on Washington Avenue at Hennepin, Nicollet or Marquette Avenues Get off at 25th and River-side 20 minutes from Loop
- I* Swedish Hospital New Building, Eighth Street at Ninth Avenue South General 320 beds  
Seating capacity 100  
Bloomington-Columbia Heights streetcar, east-bound, at Second Avenue and Fourth Street South Get off at Tenth Avenue South (10 minutes from Loop)
- J* Abbott Hospital 1717 First Avenue South 106 beds (50 pediatrics) Seating capacity 60  
Nicollet Avenue streetcar, south-bound, on Marquette Avenue, to Eighteenth Street 5 minutes from Loop Walking distance from Auditorium
- K* Northwestern Hospital 2627 Chicago Avenue General 200 beds Seating capacity 100  
Chicago Avenue streetcar, southbound, on Eighth Street South at Hennepin, Nicollet or Marquette Avenues, to 27th Street South 20 minutes from Loop
- L* Glen Lake Sanatorium Hennepin County Tuberculosis Sanatorium 700 beds (60 children)  
Seating capacity 400  
Bus at Union Bus Station, Seventh Street and First Avenue North Special bus for members of The College leaves the Nicollet Hotel at 7 45 A M and takes on passengers at Radisson, Dyckman, Curtis and Leamington Hotels

### *Note*

Hennepin, Nicollet and Marquette Avenues, the principal thoroughfares, lie approximately parallel, and are crossed by the numbered streets Washington Avenue, upon which are located the Post-Office and the Milwaukee Station, lies between Second and Third Streets Grant Street, upon which the Municipal Auditorium faces, corresponds to Thirteenth Street

The taxicab fare in the Loop district is twenty-five cents from railway stations to hotels or to the Municipal Auditorium

The taxicab care to any hospital in this city does not exceed seventy cents, with no charge for extra passengers

Bus service is provided to the Veterinary Building, University Farm and to Glen Lake Sanatorium and these leave on schedule The bus fare to the former is fifty cents round trip and to the latter seventy-five cents round trip In case taxicabs are necessary or desired, note that the rate per cab to the University Farm is \$1 30 and to Glen Lake Sanatorium \$4 00, these being independent of the number of passengers.

PROGRAM FOURTEENTH ANNUAL CLINICAL SESSION

MINNEAPOLIS COMMITTEES

S Marx White, General Chairman

EXECUTIVE COMMITTEE

S Marx White—Chairman

Henry L Ulrich

E L Gardner

Olga S Hansen—Secretary

COMMITTEE ON CONVOCAATION AND ENTERTAINMENT

J Fowler Avery—Chairman

F L Jennings

Archie Beard

Samuel A Weisman

COMMITTEE ON AUDITORIUM AND TRANSPORTATION

Charles R Drake—Chairman

Clifford E Henry

Hugo O Altnow

COMMITTEE ON CLINICS AND DEMONSTRATIONS

Henry L Ulrich—Chairman

Moses Barron

Hilding Berglund

Charles R Drake

George E Fahr

E L Gardner

F L Jennings

E S Mariette

J Arthur Myers

W A O'Brien

T A Peppard

Robert I Rizer

COMMITTEE ON HOTELS

Norman M Smith—Chairman

Frederick H K Schaaf

Arthur A Wohlrabe

COMMITTEE ON PUBLICITY

J Arthur Myers—Chairman

(Co-operating with the Committee on Publicity of the Hennepin County Medical Society)

COMMITTEE ON ENTERTAINMENT OF VISITING WOMEN

Mrs E S Mariette—Chairman

Mrs H O Altnow

Mrs J Fowler Avery

Mrs Moses Barron

Mrs Charles R Drake

Mrs George E Fahr

Mrs Everett Geer

Mrs Clifford E Henry

Mrs F. L Jennings

Mrs J Arthur Myers

Mrs Robert I Rizer

Mrs Fredk H K Schaaf

Mrs Norman M Smith

Mrs Clyde A Undine

Mrs S A Weisman

Mrs Arthur Wohlrabe

Dr Olga S Hansen

## FINAL PROGRAM

ANNUAL CLINICAL SESSION  
THE AMERICAN COLLEGE OF PHYSICIANS

February 10-14, 1930

Monday, February 10, 1930

## OPENING SESSION, 2 30 O'CLOCK

The Auditorium

## 1 Addresses of Welcome

Lotus Delta Coffman, President of the University of Minnesota  
 Elias P Lyon, Dean of the University of Minnesota Medical School  
 Edward L Tuohy, Duluth,  
 President of the Minnesota Society of Internal Medicine.  
 S H Boyer, Duluth,  
 President of the Minnesota State Medical Association  
 E L Gardner, Minneapolis,  
 President of the Hennepin County Medical Society

## 2 Reply to Addresses of Welcome

John H Musser, Jr, New Orleans,  
 President of The American College of Physicians

## 3 Colloids in Medicine

Ross A Gortner, University of Minnesota.

## 4 Cerebral Localization

Lewis J Pollock, Chicago

## 5. The Psychological Panel in Diagnosis and Prognosis

Walter Freeman, Washington, D C

## 6 Gastro-Intestinal Troubles that Now Go Undiagnosed

Walter C Alvarez, Rochester, Minn

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(Monday, February 10, 1930)

## EVENING SESSION, 8 00 O'CLOCK

The Auditorium

## 1. Latent Hyperthyroidism Masked as Heart Disease

Samuel A. Levine, Boston

## 2 Observations on the Etiology of Gall-Stones

A C Ivy, Chicago

## 3 The Significance of Atelectasis in Bronchopulmonary Conditions

Frederick T. Lord, Boston.

## 4 Moving Pictures of the Results of Stramonium Treatment in Encephalitis

Frederick Epplen, and (by invitation) A. L. Jacobson, Seattle

Tuesday, February 11, 1930

MORNING, 9 00 TO 12 00 O'CLOCK  
Clinics and Demonstrations

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AFTERNOON, 2 00 O'CLOCK

The Auditorium

VASCULAR DISEASE

- 1 The Effect of Generalized Arteriosclerosis upon the Heart and the Systematic Circulation  
George E Fahr, Minneapolis
  - 2 Some Newer Aspects in the Problem of Essential Hypertension  
Norman M Keith and James W Kernohan, Rochester, Minn
  - 3 The Retinal Vascular Changes in Hypertension  
Henry P Wagner, Rochester, Minn
  - 4 Arteriosclerosis in Diabetes  
Elliott P Joslin, Boston
  - 5 The Relations of Arterial Sclerosis and Renal Disease  
Alfred Stengel, Philadelphia
  - 6 The Causes of Arterial Hypertension  
E T Bell, Minneapolis
  - 7 The Management of Hypertension  
James S McLester, Birmingham
  - 8 The New Possibilities in Classification and Treatment of Anemia  
Hilding Berglund, Minneapolis
  - 9 Cinematographic Demonstration of Human Intestinal Protozoa Pictures and Remarks on their Biology, Pathology and Treatment  
John V Barrow, Los Angeles
- 

(Tuesday, February 11, 1930)

EVENING, 8 00 O'CLOCK

The Auditorium

- 1 History of Syphilis  
Joseph L Miller, Chicago
- 2 History of Certain Medical Instruments of Precision  
Logan Clendening, Kansas City, Mo
- 3 Spontaneous Pneumothorax, Non-tuberculous  
F J Hirschboeck, Duluth, Minn
- 4 The Healing of Tuberculosis, Illustrated by Films and Slides  
Francis M Pottenger, Monrovia, Calif

## College News Notes

Wednesday, February 12, 1930

MORNING, 9 00 TO 12 00 O'CLOCK  
Clinics and Demonstrations

AFTERNOON, 2 00 O'CLOCK

The Auditorium

- 1 Splenic Puncture as a Diagnostic Procedure in Infancy and Childhood  
Julius H Hess, Chicago
- 2 I Diagnostic and Physiologic Studies in Certain Forms of Scleroderma  
George E Brown and Paul A O'Leary, Rochester, Minn
- II Surgical Indications and Operative Results in the Treatment of Vasospastic Types  
of Scleroderma, with Sympathetic Ganglionectomy  
A W Adson, Rochester, Minn
- 3 Sympathectomy in Polyarthritis  
Leonard G Rowntree, Rochester, Minn
- 4 The Relation of Experimental Rheumatoid Inflammation to Allergy  
Benjamin J Clawson, Minneapolis
- 5 In Defense of the Stethoscope  
James B Herrick, Chicago
- 6 Rectal Temperature Curves, Normal and Abnormal  
William B Breed, Boston
- 7 The Limitations of Heliotherapy in Pulmonary Tuberculosis  
Bernard L Wyatt, Tucson
- 8 Résumé of Our Present Attitude Regarding Iodine in the Treatment of Toxic Goiter  
James H Means, Boston
- 9 Unusual Addison's Syndromes  
A B Brower, Dayton, Ohio.
- 10 A New Method for the Treatment of Pellagra  
Clyde Brooks, University, Alabama
- 11 Multiple Polyposis of the Colon  
J A Bargen, Rochester, Minn

(Wednesday, February 12, 1930)

EVENING, 8 00 O'CLOCK

The Auditorium

## CONVOCATION OF THE COLLEGE

The General Profession is cordially invited No special admission tickets are required

1 Convocation Ceremony

2 President's Address

John H Musser, Jr, New Orleans

## SMOKER

The Smoker will follow the Convocation Exercises, after a brief intermission An attractive program has been arranged.

Thursday, February 13, 1930

MORNING, 9 00 TO 12 00 O'CLOCK  
Clinics and Demonstrations

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AFTERNOON, 2 00 O'CLOCK  
The Auditorium

- 1 Symposium on The Biology of Cancer.  
The Etiology and Biology of Cancer  
Leo Loeb, St Louis  
The Nature of Heredity in Animals  
H Gideon Wells, Chicago  
Heredity of Cancer in Man  
Aldred Scott Warthin, Ann Arbor  
The Principles of Radiation Treatment  
Francis Carter Wood, New York
- 2 Undulant Fever in California  
J Edward Harbinson, Woodland, Calif
- 3 Undulant Fever, A Clinicopathological Study  
Walter M Simpson, Dayton, Ohio
- 4 Curing the Ulcer Patient  
Seale Harris, Birmingham

The General Business Meeting of The College will be held at 4 00 o'clock in the Auditorium All Masters and Fellows should attend

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Thursday, February 13, 1930

EVENING, 7 00 O'CLOCK  
The Curtis Hotel

THE ANNUAL BANQUET OF THE COLLEGE  
(Procure tickets at the Registration Bureau )

A Dance will follow the Banquet

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Friday, February 14, 1930

MORNING, 9 00 TO 12 00 O'CLOCK  
Clinics and Demonstrations

---

AFTERNOON, 2 00 O'CLOCK  
The Auditorium

- 1 Some Observations of Functional Diseases of the Alimentary Tract  
William Gerry Morgan, Washington, D C
- 2 Remarks on Chronic Infections  
Allen K. Krause, Tucson.
- 3 Symposium on The Rôle of Surgery in Pulmonary Tuberculosis  
Pneumothorax  
James Burns Amberson, Loomis, N Y



## Pneumolysis

Ralph C Matson, Portland, Ore

Multiple Intercostal Neurectomy and Phrenicectomy

John Alexander, Ann Arbor

## Thoracoplasty

Philip King Brown, San Francisco

General Consideration of the Rôle of Surgery in Tuberculosis

Gerald Webb, Colorado Springs

- 4 The Diagnosis of Pre-Clinical or Latent Tubercle by Caulfeild's Inhibitive and the T C F (with Lantern Slides of Chests and Graphs )  
W E Ogden, Toronto
- 5 A Diagnostic Triad in Syphilitic Aortitis  
C Saul Danzer, Brooklyn

## PROGRAM OF CLINICS

A Tuesday, February 11, 1930

## UNIVERSITY HOSPITALS, UNIVERSITY OF MINNESOTA

(Union and Delaware Streets, S E )

Todd Amphitheatre

(Capacity—160)

- 9 00- 9 30 Testing Gastric Function  
Hilding Berglund
- 9 30-10 00 X-ray Treatment of Hyperthyroidism  
W Stenstrom and Karl Anderson
- 10 00-10 30 Oesophagograms in Heart Diagnosis  
Leo Rigler
- 10 30-11 30 The Clinical Development of Rheumatic Heart Disease  
S A Levine, Boston
- 11 30-12 00 Circulatory Tests Previous to Amputation  
W T. Peyton

A Wednesday, February 12, 1930

## UNIVERSITY HOSPITALS, UNIVERSITY OF MINNESOTA

(Union and Delaware Streets, S E )

Todd Amphitheatre

(Capacity—160)

- 9 00- 9 30 Purpura  
Henry L. Ulrich
- 9 30-10 00 Rare Forms of Myelosis  
Hal Downey
- 10 00-10 30 Secondary Anemias.  
Hilding Berglund
- 10 30-11 00 Lymphatic Leukemia and Aplastic Anemia  
M Fallon and W. A. O'Brien
- 11 00 11 30 Syphilitic Heart Disease.  
J H Musser, New Orleans
- 11 30-12 00 Skin Clinic.  
H F. Michelson

A

Thursday, February 13, 1930

## UNIVERSITY HOSPITALS, UNIVERSITY OF MINNESOTA

(Union and Delaware Streets, S E )

Todd Amphitheatre

(Capacity—160)

- 9 00- 9 30 Coarctation of Aorta  
Henry L Ulrich
- 9 30-10 30 Scleros of Pulmonary Artery  
Henry L Ulrich and W A O'Brien
- 10 00-11 00 The Heart in Pregnancy  
S Marx White and Jennings C Litzenberg
- 11 00-11 30 Fulminating Hypertension.  
Richard Johnson and W A O'Brien
- 11 30-12 00 Congenital Heart  
M J Shapiro
- 

A

Friday, February 14, 1930

## UNIVERSITY HOSPITALS, UNIVERSITY OF MINNESOTA

(Union and Delaware Streets, S E )

Todd Amphitheatre

(Capacity—160)

- 9 00- 9 30 Endothelioma  
W A O'Brien and L G Rigler
- 9 30-10 00 Tumors of the Oesophagus  
W A O'Brien and K Phelps
- 10 00-10 30 Cancer of the Stomach  
Karl Anderson and L G Rigler
- 10 30-11 00 Cancer of the Head and Neck  
Carl Waldron
- 11 00-11 30 Cancer of the Rectum  
A C Strachauer
- 11 30-12 00 Myeloma  
H Berglund and L G Rigler
- 

A

Tuesday, February 11, 1930

## UNIVERSITY HOSPITALS, UNIVERSITY OF MINNESOTA

(Union and Delaware Streets, S E )

Eustis Amphitheatre

(Capacity—150)

- 9 00- 9 30 Ulcerative Colitis  
Karl Anderson
- 9 30-10 00 X-ray Diagnosis of Small Pleuritic Exudates  
Leo Rigler
- 10 00-10 30 Bronchiectasis  
Kenneth Phelps
- 10 30-11 30 Chronic Arthritis  
J L Miller, Chicago
- 11 30-12 00 Pancreatic Cyst  
Owen Wangenstein

B

Wednesday, February 12, 1930

## UNIVERSITY HOSPITALS, UNIVERSITY OF MINNESOTA

(Union and Delaware Streets, S E )

Eustis Amphitheatre

(Capacity—150)

- 9 00-10 00 Bowel Obstruction  
Owen Wangenstein
- 10 00-11 00 Medical Clinic  
E L Tuohy, Duluth
- 11 00-11 30 Embolectomy  
W T Peyton.
- 11 30-12 00 Treatment of Varicose Veins  
J M Hayes
- 

B

Thursday, February 13, 1930

## UNIVERSITY HOSPITALS, UNIVERSITY OF MINNESOTA

(Union and Delaware Streets, S E )

Eustis Amphitheatre

(Capacity—150)

- 9 00- 9 30 Pediatric Clinic.  
F. W Schultz
- 9 30-10 00 Hydrocephalus Treated with Diuretin  
C A Stewart
- 10 00-11 00 Pediatric Clinic  
Julius Hess, Chicago
- 11 00-11 30 Orthopedic Clinic  
W H Cole, St Paul
- 11 30-12 00 Tuberculosis in Childhood  
J A Myers
- 

B

Friday, February 14, 1930

## UNIVERSITY HOSPITALS, UNIVERSITY OF MINNESOTA

(Union and Delaware Streets, S E )

Eustis Amphitheatre

(Capacity—150)

- 9 00- 9 30 Nephrosis  
Hilding Berglund
- 9 30-10 00 Hodgkin's Disease.  
Reuben Johnson and W Stenstrom
- 10 00-10 30 The Eye in Cardio-Renal Disease  
F E Burch.
- 10 00-11 30 Vibration Sense and New Method for Its Quantitative Testing  
J C McKinley and R Gray
- 11 30-12 00 Gynecological Problems for the Internist  
Jennings C. Lutzenberg.

C

Tuesday, February 11, 1930

## INSTITUTE OF ANATOMY, UNIVERSITY OF MINNESOTA

(Washington Avenue near Church Street, S E )

Room 102, First Floor

(Capacity—226)

- 9 00- 9 30 Study of Malnutrition  
C M Jackson
- 9 30-10 00 Growth and Development  
R E Scammon
- 10 00-10 30 Innervation of Chest  
A T Rasmussen
- 10 30-11 30 Rôle of Vitamines  
G O Burr
- 11 00-11 30 Deficiency Diet and Sterility  
J A Urner
- 11 30-12 00 Problems in Hematology  
Hal Downey

C

Wednesday, February 12, 1930

## INSTITUTE OF ANATOMY, UNIVERSITY OF MINNESOTA

(Washington Avenue near Church Street, S E )

Room 102, First Floor

(Capacity—226)

- 9 00- 9 30 Carcinoid Tumors of Ileum  
Hamilton Cooke
- 9 30-10 00 Studies in Rheumatic Fever  
B J Clawson
- 10 00-10 30 Differential Diagnosis of Hodgkin's Disease, Leukemia, Lymphosarcoma  
J S McCartney
- 10 30-11 00 Recent Advances in Pharmacology  
A D Hirschfelder
- 11 00-12 00 Demonstration of Secretion of Urine in Kidney  
R N Bieter

C

Thursday, February 13, 1930

## INSTITUTE OF ANATOMY, UNIVERSITY OF MINNESOTA

(Washington Avenue near Church Street, S E )

Room 102, First Floor

(Capacity—226)

- 9 00- 9 30 Distribution of Iodin and Goiter  
J F McClendon
- 9 30-10 00 Bile Salt Determinations  
T A Pascoe and R L Gregory
- 10 00-10 30 The Allergy Problem for Internists  
W P Larson
- 10 30-11 00 Parasitology and Disease  
W A Riley
- 11 00-11 30 The Higher Fungi  
A T Henrici
- 11 30-12 00 Tularemia in Man and Animals  
R G Green

C

Friday, February 14, 1930

INSTITUTE OF ANATOMY, UNIVERSITY OF MINNESOTA  
(Washington Avenue near Church Street, S E)  
Room 102, First Floor  
(Capacity—226)

- 9 00- 9 30 Student Health Service  
H. S. Diehl
- 9 30-10 00 Studies in Tuberculosis in University Students  
J A Myers
- 10 00-10 30 Periodic Health Examination in University Students  
H D Lees
- 10.30-11 00 Hypertension Studies in University Students  
H. S. Diehl
- 11 00-11 30 Mental Hygiene in University Students  
E M deBarry
- 11 30-12 00 Infant and Maternal Hygiene  
E C Hartley.

D

Wednesday, February 12, 1930

VETERINARY BUILDING, UNIVERSITY FARM, ST PAUL  
Room 107, First Floor  
(Capacity—125)

- 9 30- 9 30 Discussion and Demonstration of Sources of Infection Through Meats  
The Staff  
(The material for this demonstration and that of the entirely new display tomorrow is made available through the cooperation of Dr G E Totten Federal Inspector in Charge, U S Department of Agriculture, Bureau of Animal Industry, South St Paul)
- 9 30-10 00 a Mechanism of Milk Secretion.  
b Demonstration of Symptoms of Hypocalcemia  
W E Peterson and W L Boyd
- 10 00-10 30 a Life Cycle of the Ascarid  
b Diagnosis of Pullorum Disease Demonstration of Life Cycle  
H C H Kernkamp
- 10 30-11 00 Animal Parasites of Man Demonstrations  
W A Riley
- 11 00-11 30 Leukemia in the Fowl Demonstration  
R Fenstermacher
- 11 30-12 00 Normal Variations in the Calcium and Phosphorus Content of the Blood  
Illustrated  
I. S. Palmer.

D

Thursday, February 13, 1930

VETERINARY BUILDING, UNIVERSITY FARM, ST PAUL  
Room 107, First Floor  
(Capacity—125)

(On display in Room 103, by Veterinary Department, is a Demonstration of Pathological Specimens obtained in Meat Inspection Relation to Human Health)

- 9 00- 9 30 Acidosis in Animals (Demonstration.)  
W L. Nelson and W L. Boyd.

- 9 30-10 00 Relation between Animal and Plant Diseases (Demonstration)  
E C Stakman
- 10 00-10 30 Infectious Abortion and Undulant Fever (Demonstration)  
C P Fitch, C R Donham and A L Delez
- 10 30-11 00 Phosphorus Deficiency (Demonstration)  
C H Eckles
- 11 00-11 30 The Corpus Luteum, the Oestrus Cycle, and the Treatment of Sterility in  
the Bovine  
W L Boyd
- 11 30-12 00 Evaluation of Dietary Materials (Illustrated)  
Alice Biester
- 

E

Tuesday, February 11, 1930

## HENNEPIN COUNTY MEDICAL SOCIETY ROOMS

20th Floor, Medical Arts Building

(Ninth Street South between Nicollet and Marquette Avenues)  
(Capacity—350)

- 9 00- 9 30 Diabetic Coma  
Donald McCarthy
- 9 30-10 00 Medical Clinic  
F J Hirschboeck, Duluth
- 10 00-10 45 Medical Clinic  
J S. McLester, Birmingham
- 10 45-11 30 Physiology of Liver  
F C Mann, Rochester, Minn
- 11 30-12 00 Riedel's Struma followed by Myxedema  
Charles N Hensel, St Paul
- 

E

Wednesday, February 12, 1930

## HENNEPIN COUNTY MEDICAL SOCIETY ROOMS

20th Floor, Medical Arts Building

(Ninth Street South between Nicollet and Marquette Avenues)  
(Capacity—350)

- 9 00- 9 30 Toxic Myocardium  
Morris Nathanson
- 9 30-10 00 Hypothyroidism  
F H K. Schaaf
- 10 00-10 45 Medical Clinic  
J H Means, Boston
- 10 45-11 15 Broncho-Oesophageal Fistula, Diehl's Crisis  
Moses Barron
- 11 15-12 00 Moving Pictures, Results of Sympathectomy in Chronic Arthritis  
L G Rowntree, Rochester, Minn.

E

Thursday, February 13, 1930

HENNEPIN COUNTY MEDICAL SOCIETY ROOMS  
20th Floor, Medical Arts Building  
(Ninth Street South between Nicollet and Marquette Avenues)  
(Capacity—350)

- 9 00- 9 30 Bronchial Asthma  
A E Cardle
- 9 30-10 00 Addison's Disease  
Reuben Johnson
- 10 00-11 00 Sensory Disturbances, Their Recognition and Significance  
Walter Freeman, Washington, D C.
- 11 00-11 30 Clinic in Hematology, Atypical Lymphoid Reactions, Blood Platelet  
Dyscrasias  
Edgar T Hermann, St Paul
- 11 30-12 00 Amyloid Disease  
Harry Oerting, St Paul
- 

E

Friday, February 14, 1930

HENNEPIN COUNTY MEDICAL SOCIETY ROOMS  
20th Floor, Medical Arts Building  
(Ninth Street South between Nicollet and Marquette Avenues)  
(Capacity—350)

- 9 00- 9 30 Surgical Treatment of Diabetes  
Macnider Wetherby
- 9 30-10 00 Evulsion of Phrenic Nerve in Tuberculosis  
E K Geer, St Paul
- 10 00-11 00 Chronic Sinus Infection in Relation to Systemic Disease  
Noble Wiley Jones and F B Kistner, Portland, Ore
- 11 30-11 30 Arterial Hypertension  
J A Lepak, St Paul
- 11 30-12 00 Hypothyroidism  
Charles N Hensel, St Paul
- 

F

Tuesday, February 11, 1930

MINNEAPOLIS GENERAL HOSPITAL  
(Fifth Street between Sixth and Seventh Avenues)  
Sun Porch, First Floor  
(Capacity—125)

- 9 00- 9 15 Clinic on Leukemia  
Moses Barron
- 9 15-10 30 Neurological Diagnosis  
Lewis J Pollock, Chicago
- 10 30-11 00 Clinic on Hypothyroidism  
I H K Schind
- 11 00-12 00 Clinic on Gastro-Intestinal Disease  
F L Gardner

F

Wednesday, February 12, 1930

MINNEAPOLIS GENERAL HOSPITAL  
(Fifth Street between Sixth and Seventh Avenues)  
Sun Porch, First Floor  
(Capacity—125)

- 9 00-10 00 Clinic on Neurosyphilis  
J C Michael  
10 00-11 00 Chest Clinic  
T A Peppard  
11 00-12 00 Clinic on Anemia  
J Davis

F

Thursday, February 13, 1930

MINNEAPOLIS GENERAL HOSPITAL  
(Fifth Street between Sixth and Seventh Avenues)  
Sun Porch, First Floor  
(Capacity—125)

- 9 00-10 0 Clinic on Leukemia  
Moses Barron  
10 00-11 00 Clinic on Ramisectionomy  
A. A. Zierold  
11 00-12 00 Clinic Heart Disease in Pregnancy  
M Nathanson

F

Friday, February 14, 1930

MINNEAPOLIS GENERAL HOSPITAL  
(Fifth Street between Sixth and Seventh Avenues)  
Sun Porch, First Floor  
(Capacity—125)

- 9 00-10 00 Clinic on Toxic Myocardium  
M Nathanson  
10 00-11 00 Clinic on Gastro-Intestinal Diseases  
E L Gardner  
11 00-12 00 Clinic on Syphilis and Skin Diseases  
S Sweitzer

G

Tuesday, February 11, 1930

MINNEAPOLIS GENERAL HOSPITAL  
(Fifth Street, between Sixth and Seventh Avenues)  
Clinic Room, Basement Floor  
(Capacity—70)

- 9 00-10 00 Erysipelas Treatment Comparative Study of more Recent Methods  
W. Ude  
10 00-10 30 Clinical Pathological Conference on Rheumatic Fever Pneumonia  
N Lufkin and A Kerkhof  
10 30-12 00 Clinic on Varicose Ulcers with Demonstration of Pathology  
H O McPheeters and N Lufkin



G

Wednesday, February 12, 1930

MINNEAPOLIS GENERAL HOSPITAL  
(Fifth Street, between Sixth and Seventh Avenues)  
Clinic Room, Basement Floor  
(Capacity—70)

- 9 00-10 00 Crystallization of Our Knowledge of Childhood Tuberculosis  
J A Myers  
10 00-11 00 Clinical Pathological Conference on Hodgkin's Disease with Pel Ebstein Fever  
J Davis and N Lufkin  
11 00-12 00 Clinical Pathological Conference on Kidney Disease  
E T Bell and G E Fahr
- 

G

Thursday, February 13, 1930

MINNEAPOLIS GENERAL HOSPITAL  
(Fifth Street, between Sixth and Seventh Avenues)  
Clinic Room, Basement Floor  
(Capacity—70)

- 9 00- 9 30 X-ray Diagnosis of Tuberculosis of Chest  
W Ude  
9 30-10 00 Surgical Treatment of Ulcerative Colitis  
O J Campbell  
10 00-11 30 Clinic on Varicose Ulcers with Demonstration of Pathology  
H O McPheeters and Dr Lufkin  
11 30-12 00 Conservative Treatment of Diabetic Gangrene  
E Regnier
- 

G

Friday, February 14, 1930

MINNEAPOLIS GENERAL HOSPITAL  
(Fifth Street, between Sixth and Seventh Avenues)  
Clinic Room, Basement Floor  
(Capacity—70)

- 9 00-10 00 X-ray Methods in Heart Diagnosis  
W Ude  
10 00-11 00 Clinical Pathological Conference on Miliary Tuberculosis following Renal Tuberculosis  
J. C. Davis and N Lufkin  
11 00-12 00 Clinical Pathological Conference on Renal Disease  
E T Bell and G E Fahr
- 

H

Tuesday, February 11, 1930

ST MARY'S HOSPITAL  
(2500 South Sixth Street)  
Assembly Room  
(Capacity—400)

- 9 00- 9 30 Pediatric Clinic  
I S Platou  
9 30-10 00 Types of Gastro-Intestinal Neuroses  
Walter C Alvarez, Rochester, Minn

- 10 30-11 30 Clinic on Diseases of Respiratory Tract  
Frederick T Lord, Boston
- 11 30-12 00 Coronary Arterial Disease  
M H Nathanson

H Wednesday, February 12, 1930

ST MARY'S HOSPITAL  
Assembly Room  
(Capacity—400)

- 9 00- 9 30 Cancer of the Stomach, Syphilis of the Stomach  
9 30-10 00 Ophthalmoscopic Examination in General Medicine  
Walter Fink
- 10 00-11 00 Diseases of the Colon  
J A Bargen, Rochester, Minn
- 11 00-11 30 Subarachnoid Hemorrhage of Undetermined Origin  
A S Hamilton
- 11 30-12 00 Thrombangeitis Obliterans  
H T Evans

H Thursday, February 13, 1930

ST MARY'S HOSPITAL  
(2500 South Sixth Street)  
Assembly Room  
(Capacity—400)

- 9 00- 9 30 Exophthalmic Goiter with Exceptional Heart Findings, Report of Case  
Stanley Maxeiner.
- 9 30-10 00 Present-Day Management of Hyperthyroidism  
Leo Murphy
- 10 00-11 00 Essential Hypertension  
W B Breed, Boston
- 11 00-11 30 Differential Diagnosis in the Upper Urinary Tract  
T H Sweetser
- 11 30-12 00 Study of Differential Diagnosis of Head Pains, Presentation of Cases  
C D Wright

H Friday, February 14, 1930

ST MARY'S HOSPITAL  
(2500 South Sixth Street)  
Assembly Room  
(Capacity—400)

- 9 00- 9 30 Diabetes  
Donald McCarthy
- 9 30-10 00 Appendicitis in Early Pregnancy
- 10 00-11 00 Undulant Fever and Tularemia  
Walter M Simpson, Dayton, Ohio
- 11 00-11 30 Reactive Depression  
J C Michael
- 11 30-12 00 Obscure Back Cases  
M O Henry

*I*

Tuesday, February 11, 1930

SWEDISH HOSPITAL, NEW BUILDING  
(Eighth Street at Ninth Avenue South)  
Clinical Laboratories, Third Floor  
(Capacity—100)

- 9 00- 9 30 Review of 200 Cases of Functional Gall Bladder Study  
G T Nordin  
9 30-10 00 Childhood Tuberculosis  
C A Stewart  
10 00-10 30 Cancer Therapy with Special Reference to Metastases  
Charles R Drake  
10 30-11 00 Sequelae of Head Injuries  
Julius Johnson  
11 00-11 30 Myasthenia Gravis with Dilatation of Duodenum  
A S Hamilton  
11 30-12 00 Duodenal Stasis and Obstruction  
C B Wright

*J*

Wednesday, February 12, 1930

ABBOTT HOSPITAL  
(1717 First Avenue South)  
(Capacity—60)

- 9 00- 9 15 Presentation of Cases (Lantern)  
F C Rodda  
9 15- 9 30 Aspiration Method for Treatment of Laryngeal Diphtheria  
E S Platou  
9 30-10 00 Presentation of Cases  
F. W Schlutz  
10 00-10 15 Presentation of Cases  
E R Robb  
10 15-10 30 Presentation of Cases  
Rood Taylor  
10 30-10 45 Presentation of Cases  
N O Pearce  
10 45-11 00 Intraperitoneal Transfusion  
David Siperstein  
11 00-12 00 Tuberculosis and Bronchiectasis Laryngeal Cases  
Chester A Stewart

*J*

Thursday, February 13, 1930

ABBOTT HOSPITAL  
(1717 First Avenue South)  
(Capacity—60)

- 9 00- 9 15 Presentation of Cases  
E J Hueneke  
9 15- 9 30 Presentation of Cases  
Cecile Moriarty  
9 30- 9 45 Pseudo-Muscular Dystrophy  
Edward Dyer Anderson

- 9 45-10 00 Functional Disturbances of Pre-School Child  
Grete Seham
- 10 00-10 30 Functional Disturbances of School Child  
Max Seham
- 10 30-11 00 Skin Diseases (Lantern Slides)  
Henry Michelson
- 11 00-12 00 X-ray Studies of Children  
R G Allison

J

Friday, February 14, 1930

SWEDISH HOSPITAL, NEW BUILDING  
(Eighth Street at Ninth Avenue South)  
Clinical Laboratories, Third Floor  
(Capacity—100)

- 9 00- 9 30 Radiation Therapy of Cancer of Prostate  
G T Nordin
- 9 30-10 00 Bronchiectasis  
C A Stewart
- 10 00-11 00 Medical Clinic  
C Saul Danzer, Brooklyn
- 11 00-11 30 Medical Cases Illustrating the Method of Defense of the Body  
S P Rees
- 11 30-12 00 New Methods of Study of Gastric Secretion, Especially with Histamin and Alcohol  
C B Wright

K

Tuesday, February 11, 1930

NORTHWESTERN HOSPITAL  
(Chicago Avenue and Twenty-Seventh Street)  
First Floor  
(Capacity—100)

- 9 00- 9 30 Hearing in Relation to Medicine  
H Newhart
- 9 30-10 00 X-ray in Medicine  
R G Allison.
- 10 00-10 45 Arthritis  
L G Rowntree, Rochester, Minn
- 10 45-11 30 The Non-Tuberculous Chest  
T A Peppard
- 11 30-12 00 Pulmonary Tuberculosis  
Everett K Geer, St Paul

K

Wednesday, February 12, 1930

NORTHWESTERN HOSPITAL  
(Chicago Avenue and Twenty-Seventh Street)  
First Floor  
(Capacity—100)

- 9 00- 9 30 Vascular Surgery  
A A Zierold

- 9 30-10 00 Diabetes  
Franklin Adams, Rochester, Minn
- 10 00-11 00 Diabetes  
E P Joslin, Boston
- 11 00-12 00 Diabetes  
R M Wilder, Chicago

K

Friday, February 14, 1930

NORTHWESTERN HOSPITAL  
(Chicago Avenue and Twenty-Seventh Street)  
First Floor  
(Capacity—100)

- 9 00- 9 30 Carbon Dioxide-Oxygen Studies in Anesthesia  
A T Mann
- 9 30-10 00 Vincent's Infection from the Dental Standpoint  
Benjamin Sandy
- 10 00-11 00 Vincent's Infection  
R I Rizer
- 11 00-11 30 Tuberculosis of the Rectum  
W A Fansler
- 11 30-12 00 Thoracic Surgery in Tuberculosis  
A A Law

L

Tuesday, February 11, 1930

GLEN LAKE SANATORIUM  
(Twelve miles from the Auditorium Take Excelsior Blvd )  
Assembly Room  
(Capacity—500)

- 9 00- 9 30 Childhood Tuberculosis  
P M Mattill
- 9 30-10 00 Diagnosis of Tuberculosis  
Francis M Pottenger, Monrovia, Calif
- 10 00-10 30 Collapse Therapy in Pulmonary Tuberculosis  
T J. Kinsella
- 10 30-11 00 X-ray in Diagnosis and Treatment of Pulmonary Tuberculosis  
Malcolm Hanson, Minneapolis
- 11 00-11 30 Heliotherapy in Pulmonary and Extra-Pulmonary Tuberculosis  
C W Mills, Tucson
- 11 30-12 00 Intestinal Tuberculosis  
V K Funk

M

Wednesday, February 12, 1930

GLEN LAKE SANATORIUM  
(Twelve miles from the Auditorium Take Excelsior Blvd )  
Assembly Room  
(Capacity—500)

- 9 00- 9 30 General Management of Pulmonary Tuberculosis  
E. S. Mariette
- 9 30-10 00 Genito-Urinary Tuberculosis  
Gilbert J. Thomas, Minneapolis

- 10 00-10 30 Diagnosis of Childhood Tuberculosis  
Gerald B Webb, Colorado Springs
- 10 30-11 00 Heliotherapy in the Treatment of Tuberculosis  
C K Petter
- 11 00-11 30 Pathogenesis of the Tubercle  
H E Robertson, Rochester, Minn
- 11 30-12 00 Pregnancy and Tuberculosis  
F L Jennings

L

Thursday, February 13, 1930

## GLEN LAKE SANATORIUM

(Twelve miles from the Auditorium Take Excelsior Blvd)

Assembly Room

(Capacity—500)

- 9 00- 9 30 General Management of Pulmonary Tuberculosis  
E S Mariette
- 9 30-10 00 Pneumothorax Studies in Tuberculosis  
James Burns Amberson, Loomis, N Y
- 10 00-10 30 Orthopedic Surgery in Tuberculosis  
E P K. Fenger
- 10 30-11 00 Effect of Upper Respiratory Infection on Tuberculosis  
S Cohen
- 11 00-11 30 Selection of Cases for Cauterization of Adhesions  
Ralph C Matson, Portland, Ore
- 11 30-12 00 Thoracoplasty  
T J Kinsella

L

Friday, February 14, 1930

## GLEN LAKE SANATORIUM

(Twelve miles from the Auditorium Take Excelsior Blvd)

Assembly Room

(Capacity—500)

- 9 00- 9 30 Extra-Pulmonary Tuberculosis  
E P K Fenger
- 9 30-10 00 Thoracoplasty  
John Alexander, Ann Arbor
- 10 00-10 30 Intestinal Tuberculosis  
V K. Funk
- 10 30-11 00 Relation of Proctology to Tuberculosis  
W A Fansler, Minneapolis
- 11 00-11 30 Childhood Tuberculosis  
Philip King Brown, San Francisco
- 11 30-12 00 Pregnancy and Tuberculosis  
F L Jennings

sengers at the Radisson, Dyckman, Curtis and Leamington Hotels. The round trip fare is fifty cents. Taxicab fare is \$1.30 per cab, which can accommodate five persons. The time is about twenty-five minutes.

### SPECIAL CLINICS AND DEMONSTRATIONS AT THE UNIVERSITY FARM

Minnesota is an agricultural state. Its life depends largely upon the growing of grain and the raising of livestock. The Department of Agriculture and Home Economics is exceptionally important at the State University and includes an outstanding Division of Veterinary Medicine.

The Chief of this division, Dr. C. P. Fitch, with an unusual sense of both clinical and scientific values, has arranged a program of exceptional interest, choosing the experts in pathology, biochemistry, parasitology, nutrition and endocrinology from the entire College of Agriculture and Home Economics.

The opportunities for animal experimentation are unbounded in such an institution. Many of its problems exactly parallel those of clinical medicine. The subjects and speakers for these morning sessions of clinics and demonstrations have been chosen because of their direct bearing on the practice of medicine.

What has the work on animals taught that can be applied to the human patient? Both the practical and the academic phases have been given full attention and the short and well-pointed talks are all accompanied by illustrations or demonstrations.

What do you know about the chemistry of milk production? Would you be interested in seeing a large mammary gland through which is pumped by motor different solutions and from which is obtained milk of all colors and consistencies?

What do you know about the life-cycle of animal parasites? Would you care to see it demonstrated in all its phases, under circumstances where observation is accurate and infallible?

Did you know that acidosis occurs in animals, and that hypocalcemia gives a characteristic clinical picture? What are the normal

variations in the calcium and phosphorus content of the blood and what are the signs of phosphorus deficiency? These conditions have been produced and studied in large mammals, with metabolic processes similar to those of the human patient, by biochemists, nutritional experts and clinical veterinarians, who are reporting an epitome of their findings.

Can you recognize a case of undulant fever? Do you know how this disease is related to infectious abortion in dairy herds which veterinarians have been studying extensively for years before clinicians in general realized that undulant fever was a disease entity?

What is the present status of knowledge in regard to the relation of the corpus luteum to the oestrus cycle? This is to be discussed from the standpoint of sterility and its treatment in the bovine.

The local committee takes pride in offering these two unusual and stimulating programs to The College on Wednesday and Thursday mornings. The seating capacity is limited to 125. Special busses to the University Farm, where these programs are given, will leave the Nicollet Hotel at 7:45 a. m., stopping for passengers at the Radisson, Dyckman, Curtis and Leamington Hotels.

Praxagoras, of Cos, about three hundred years B. C., first recognized that pulsation occurred only in the arteries, although he believed that the pulsation was due to an aeriform fluid, a sort of pneuma.

Antonio Scarpa, born in Friuli in 1747, was the first to regard arteriosclerosis as a lesion involving the inner coats of the arteries. The century and a half elapsing since Scarpa began to write has shown progress in our knowledge of the arteries exceeding many fold that of the twenty-one centuries separating him from Praxagoras.

It would seem that we ought to know now all there is to know about the arteries and their diseases, but new methods and their diseases, but new methods and new points of view have greatly increased our knowledge in recent decades. While vascular disease is not covered in our program

in symposium form, a group of seven papers, each by a master in his field, has been brought together and will be read on Tuesday afternoon

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The Annual Banquet of The College will be held at 7 00 o'clock Thursday evening, February 13, at the Curtis Hotel. All physicians of the Twin Cities and vicinity and visitors attending the session are invited, with their ladies, by the members of The College and its officers to attend this Banquet. Music will be furnished and an address delivered.

Following the Banquet the dance will occur and all are invited to remain.

Tickets for the Banquet, including the dance, are \$5 00 per person and these must be purchased at the Information Bureau before 10 00 o'clock Thursday morning.

#### CONVOCATION OF THE COLLEGE 8 00 o'clock Wednesday Evening, February 12, in The Auditorium

All Fellows of The College and those to be received in Fellowship should be present. Newly elected Fellows who have not yet been received in Fellowship are requested to occupy the central section of seats especially reserved for them.

The Convocation is open to physicians generally and to such of the general public as may be interested.

Following the Convocation Ceremony, the President, Dr. John H. Musser, Jr., of New Orleans, will deliver the annual address to the Masters, Fellows and Associates of The College.

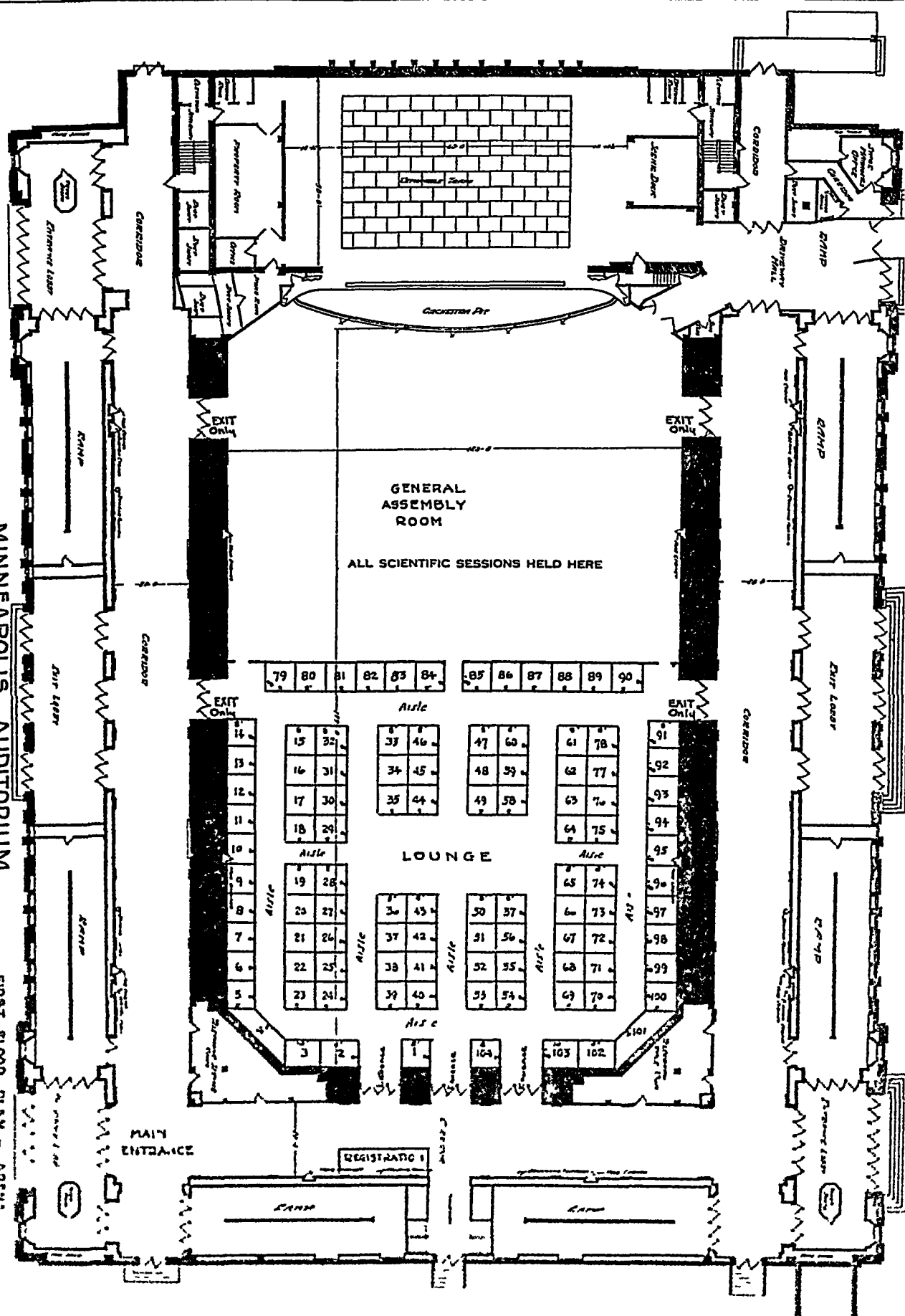
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The Smoker will follow the Convocation after a short intermission. An attractive program has been arranged. All physicians with their ladies and friends are invited.



# MINNEAPOLIS AUDITORIUM

FIRST FLOOR PLAN - AREA A



PLAN OF MINNEAPOLIS AUDITORIUM

showing layout of meeting hall, exhibits, registration, etc. The Exhibit and Exposition of medical appliances and apparatus, books, pharmaceutical products, special foods, etc will be a special feature of the Clinical Session, February 10-14, 1930

## EXPOSITION AND EXHIBITS

The plan of the Minneapolis Auditorium and the arrangement of the exhibits printed on the preceding page show the unusually fine arrangements that have been made for the Minneapolis Clinical Session. The exhibits will be highly diversified in their variety, and will bring to the attendants at the Clinical Session, the latest and most improved equipment, the best pharmaceutical products, almost the whole library of medical publications, and many other products of especial interest to the internist, pediatrician, neurologist, psychiatrist, radiologist and research worker.

This Exhibit will surpass in size, diversity and popularity any yet conducted by the College. In the midst of exhibits will

be located a large and attractive lounge, or lobby, where the attending physicians may rest, visit and hobnob together. There will be comfortable chairs and davenport, writing desks, a public stenographer and other conveniences in the Lounge for the doctors. Besides, the College will have its own booth here where information will be given, the daily bulletin announced, the daily registration and directory posted, and the publications and activities of the College displayed.

The Joseph T. Griffin Decorating Company of Louisville, Ky., who install the exhibits for the American Medical Association, the Southern Medical Association, the American Hospital Association and other prominent societies, will be in charge of the installation of booths and decoration.

Space	Exhibitor	Address
3	Abbott Laboratories	North Chicago, Ill
81 & 82	American X-Ray Corporation	Chicago, Ill
39	Anderson Company, C. F.	Minneapolis, Minn
34	Battle Creek Food Company	Battle Creek, Mich
4	Blakiston's Son & Co., P.	Philadelphia, Pa
30 & 31	Borden Sales Company	New York, N. Y.
59	Boulitte & Company, G.	New York, N. Y.
70	Britesun, Inc.	Chicago, Ill
74	Brown & Day, Inc.	St. Paul, Minn
84	Cambridge Instrument Co.	New York, N. Y.
2	Cameron's Surgical Specialty Co.	Chicago, Ill
51	Carrick Company, G. W.	Newark, N. J.
103	Chippewa Springs Corporation	Minneapolis, Minn
9	Dahl Company, Joseph E.	Minneapolis, Minn
33	Davies Rose & Co., Ltd.	Boston, Mass
53	Davis Company, F. A.	Philadelphia, Pa
42	Davis Sales Company, R. B.	Hoboken, N. J.
32	Diamond-Union Stamp Works	Boston, Mass
18	Doak Company, Inc., J.	Cleveland, Ohio
86	Gerber Products Division	Fremont, Mich
102	Gradwohl Laboratories	St. Louis, Mo
35 & 44	Hoeber, Inc., Paul B.	New York, N. Y.
55	Horlick's Malted Milk Corporation	Racine, Wis
46	Kalak Water Co.	New York, N. Y.
85	Kellogg Company	Battle Creek, Mich
87	Laboratory Products Company	Cleveland, Ohio
57	LaMotte Chemical Products Company	Baltimore, Md
50	Lea & Febiger	Philadelphia, Pa
69	Lederle Antitoxin Laboratories	New York, N. Y.
101	Lippincott Co., J. B.	Philadelphia, Pa

I	Macmillan Company, The	New York, N Y
41	Mead Johnson Co	Evansville, Ind
26	Medical Case History Bureau	New York, N Y
58	Medical Protective Co	Chicago, Ill
52	Mellin's Food Company	Boston, Mass
56 & 66	Merck & Company	Rahway, N J
15 & 16	Merrell Co, The William S	Cincinnati, Ohio
36 & 43	Metz Laboratories, Inc, H A	New York, N Y
19	Mosby Company, C V	St Louis, Mo
40	Nelson & Sons, Thomas	New York, N Y
47, 48 & 49	Petrolagar Laboratories, Inc	Chicago, Ill
37 & 38	Physicians & Hospitals Supply Co	Minneapolis, Minn
54	Sanborn Company	Cambridge, Mass
29	Saunders Company, W B	Philadelphia, Pa
10	Spencer Lens Company	Buffalo, N Y
56	Squibb & Sons, E R	New York, N Y
28	Swan-Myers Company	Indianapolis, Ind
60	Tailby-Nason Company	Cambridge, Mass
27	Taylor Instrument Companies	Rochester, N Y
45	Upsher Smith, Inc	Minneapolis, Minn
61, 62, 63 64,		
75, 76, 77 & 78	Victor X-ray Corporation	Chicago, Ill
36 & 43	Winthrop Chemical Co, Inc	New York, N Y
24	Wood & Company, William	New York, N Y

### SIDE LIGHTS ON THE EXHIBITS

C F Anderson Co, Inc, of Minneapolis, Minnesota, will occupy spaces 67 and 68 in the exhibition to be held in the Minneapolis Auditorium, February 10 to 14, inclusive.

They invite their friends to view their exhibit, which will be complete and of interest to all members of the American College of Physicians.

P Blakiston's Son & Co, Inc—Books are the tools of the physicians and every member of the American College of Physicians should allot sufficient time for a careful examination of publishers' exhibits. We shall offer this year a number of valuable new monographs. Visit our Booth, No 4. Name the subjects in which you are particularly interested at present.

The Boulton Company of New York and Paris, makers of Scientific Instruments since 1875, will exhibit and demonstrate in Booth No 59, the BOLLIFIT Electrocardiograph, portable and standard models, Pickon's Oculometer, several types of blood pressure cuffs as well as a number of physiological instruments.

PHYSIOTHERAPY IS A DEFINITE PART OF MEDICINE—"It is our most modern Therapeutic Agent, it is an indispensable part of Medical and Surgical practice. It should be used as one of the triad of Medicine, Surgery and Physical Therapy." BRITESUN, Inc, Booth No 70.

At the exhibit of Brown & Day, Inc, of St Paul, will be displayed a comprehensive line of instruments of precision and supplies required by the Internist in his daily routine. Also a battery of American Sterilizers, specially built for office and Clinic use.

The Cambridge Instrument Co, Inc, pioneer manufacturers of the Electrocardiograph, will exhibit their latest model Electrocardiographs incorporating a number of recent improvements. Other Physiological Instruments of interest to the medical profession will be shown.

The value of 'High Visibility in Diagnosis and Surgery' as applied to all phases of major and minor diagnostic, operative and therapeutic procedure will be fully demonstrated at the clinical exhibitions of

Cameron's Surgical Specialty Company, Chicago, Booth No 2 The demonstration of Cameron's Cauteries will also be a unique feature of the exhibit

Space 103—Exhibit of the Chippewa Springs Corporation of Chippewa Falls, Wisconsin, to consist of a hollow pyramid of the bottled Chippewa products—Spring Water, Carbonated Water and Dry Ginger Ale, having flood lights inside the pyramid thrown onto the bottles This is to be surrounded by a counter over which the Chippewa Natural Spring Water will be served and where chemical tests and other interesting demonstrations will prove the Chippewa slogan, "The Purest and softest Natural Spring Water in the World" This will be a truly beautiful and instructive display

Joseph E Dahl, of Minneapolis, Minnesota, showing at Booth No 9, inaugurated a special all night and holiday service to physicians six years ago which has been used by the majority of them in this vicinity, and at this time can supply any item which is needed by the profession

The distribution of Invertose for obliteration of varicose veins has been handled by this firm in the United States, and recently they have taken over the sales of McIntosh Electrical equipment for the Minnesota territory

Physicians interested in the treatment of trigeminal neuralgia should visit Booth No 33 There, Davies, Rose & Co, Ltd, Boston, Mass, will exhibit a preparation used in the relief of pains affecting the area of the fifth nerve, and which preparation is engaging widespread attention

Cardiologists, also, will find it profitable to visit this booth, as the firm will present a product of particular interest to them, too

Visiting physicians and their friends are invited to stop at Booth No 42, where they may secure full information relative to the nature and amount of the food elements present in Cocomalt—also to judge of its quality and flavor

The booth will be in charge of Miss Elsie Stark, of the R B Davis Company, Hoboken, N J

Dimond-Union Stamp Works of Boston will have an interesting exhibit at Booth No 32 of anatomical chart rubber stamps, which make diagnostic or pathological records accurate, graphic and simple

DIASPORALS—The progressive physician is particularly interested in Colloidal Therapy At Booth No 18, interesting literature on the Therapeutic application of Colloidal preparations in the treatment of Lues, Anemia, chronic Arthritis and Carcinoma should commend itself to the Therapist

Gerber's Strained Vegetables, consisting of Strained Vegetable Soup, Strained Carrots, Strained Spinach, Strained Peas, Strained Tomatoes, Strained Green Beans and Strained Prunes, all packed in 4½ ounce tins These products are unseasoned, and in addition to convenience, accuracy, and safety in providing the necessary vegetable supplement to the baby's milk diet, are also useful in a wide variety of special diet cases See them in Booth No 86

THE GRADWOHL SCHOOL OF LABORATORY TECHNIQUE—This exhibit will show methods of teaching laboratory technique, with particular reference to the Schilling method Thick drops, Giemsa-Stained blood smears, Guttaphots showing various diseases, will be shown

Paul B Hoeber, Inc, will show their entire line of medical publications and will exhibit for the first time the following book which should be of special interest to the members of the American College of Physicians "The Creed of A Biologist" by Aldred Scott Warthin Dr Warthin's book on "Old Age," published in 1929, was shown for the first time at the Boston meeting, and created great interest

Among other books of particular interest to the members of the College will be shown Simpson's "Tularemia," Pardee's "Clinical Aspects of the Electrocardiogram," Alvarez's "Mechanics of the Digestive Tract," Roth's "Cardiac Arrhythmias," Heberden's "Introduction to the Study of Physic" (edited by LeRoy Crummer and now for the first time published), and the recently issued "Outline of Preventive Medicine" published under the auspices of the

New York Academy of Medicine With two booths, this house will this year have ample room for visitors, and it is hoped that no member will overlook Booth Nos 35 and 44

Horlick's Malted Milk Corporation will be among the exhibitors at the meeting of the American College of Physicians, and plans unusual activities in the interests of its products, Horlick's the Original Malted Milk, natural and chocolate flavor, powder and tablet form and Horlick's Milk Modifier, a maltose and dextrin product The Horlick exhibit will occupy Booth No 55

Kalak, the strongest non-laxative alkaline water of commerce, will be found at Booth No 46—and attending physicians are invited to visit the booth and test the palatability of this dependable alkalinizing agent

Kalak Water is offered for therapeutic use under the guidance of the physician only

Doctors who are interested in a non-stimulating coffee for use in special diets are invited to visit the Kellogg Company exhibit at the Minneapolis Auditorium Kaffee Hag Coffee will be demonstrated and served with muffins made from Kellogg's All-Bran

Kaffee Hag is real coffee from which 97 per cent of the caffeine and indigestible wax has been removed Diet literature and pads of Prescribed Diet Lists will be distributed

WHAT IS S M A ?—It is generally accepted by physicians trained in the care and feeding of infants that the next best substitute for breast milk is some modification of cow's milk However, the degree of modification of cow's milk in the majority of cases determines the probability of success and to that end the Babies' and Children's Hospital of Cleveland have modified cow's milk to a remarkable degree and called that modification S M A

S M A is therefore, a modification of cow's milk in which the fat, protein, carbohydrate and salt content are adjusted in such a way as to produce a mixture that resembles breast milk in its essential, physical, chemical and metabolic properties

C M A is produced exclusively by The Laboratory Products Company, and you may

obtain full details concerning this product from their representatives in Booth No 87

At Booth No 57, LaMotte Simplified Blood Chemistry Apparatus will be demonstrated and all of the new and improved units will be shown These include outfits for Blood Sugar, Urine Sugar, Blood Urea, Blood Chlorides, Blood Cholesterol, Blood Calcium-Phosphorus, Blood Bilirubin, Phenolsulfonphthalein Renal Function Test, Hemoglobin, Blood pH, Urinalysis, Urine pH, Icterus Index, Blood Creatinine, Gastric Acidity, Uric Acid, Blood Bromides and Alveolar Air It is hoped that all those physicians who are interested in blood chemistry will take an opportunity to visit this exhibit The booth will be in charge of chemists who will be glad to discuss your problems with you

Lea & Febiger, at Booth No 50, will have a number of new books and new editions, and will be glad to show them Eberts—Surgical Diseases of the Thyroid Gland, Faust's Human Helminthology, Hess—Rickets Including Osteomalacia and Tetany, Gershenfeld's Bacteriology and Sanitary Science, Hill's Manual of Proctology, Jelliffe & White—Diseases of the Nervous System, Joslin's Treatment of Diabetes Mellitus, Joslin's Diabetic Manual, Kuntz on the Autonomic Nervous System, Laboratory Methods of the U S Army, Mulliner's Mechano-therapy, Park, Williams & Krumwiede on Pathogenic Microorganisms, Pemberton's Arthritis and Rheumatoid Conditions, Schafer's Essentials of Histology, Smith & Wikoff's Materia Medica, Starling's Principles of Human Physiology, Stone's The New Born Infant, Thomas' Dietary of Health and Disease

J. B. Lippincott Company are introducing six outstanding authors in their new EVERY DAY PRACTICE SERIES under the Editorship of Dr Harlow Brooks of New York City This newest enterprise, along with other new and standard works in late editions, is still being shown in a novel, attractive setting You will find the Lippincott display quite out of the ordinary, and you are invited to make it a place for meeting your friends

Whatever your specialty of Internal Medicine, visit the Macmillan Booth No 1. There you will find monographs dealing with subjects of current medical interest: Eyster's *VENOUS PRESSURE*, one of Macmillan Medical Monographs, Friedenwald's *PATHOLOGY OF THE EYE*, Parsonnet and Hyman's *APPLIED ELECTROCARDIOGRAPHY*, Rolleston's *LIFE OF SIR THOMAS CLIFFORD ALLBUTT*, the Fourth Edition of McCollum and Simmond's *THE NEWER KNOWLEDGE OF NUTRITION*, Bucky's *GRENZ RAY THERAPY*, and *THE CAMBRIDGE COMPARATIVE PHYSIOLOGY SERIES* are but a few of the important titles on display.

A well balanced food compound which meets the nutritional requirements of infants and in many cases has met the problem presented by milk protein idiosyncrasy, is offered in Mead's newest product—Sobee. Thus as well as Mead's Viosterol (originally Acterol) and the complete group of the better known Mead Infant Diet Materials will be on display at the Mead Johnson Company exhibit, Booth No 41.

A Patient's History and Accounting System Endorsed and used by Many of the Foremost Physicians in America—The Medical Case History Bureau of New York City will display and demonstrate what leading physicians consider the most complete and efficient system for every branch of medicine—recording every phase of office and home calls. The only system of its kind—made to suit your most exacting individual requirements, yet low priced.

All members of the American College of Physicians and friends are cordially invited to visit Booth No 58 of the Medical Protective Company. Mr A B Garber of the Home Office in Chicago and Mr E E Patrick, General Agent of Minnesota, will be delighted to have you call, whether merely to say "hello" and renew old acquaintances or to satisfy yourself on some question of malpractice protection. Consider them at your service and feel free to call upon them for anything which may contribute to mak-

ing this the most pleasant and successful meeting you have ever attended.

The extraordinary interest in Mellin's Food, as applied to illness of adults, that developed during the last session of the American College of Physicians, offers much encouragement to go into further details in regard to the nutritive value of Mellin's Food and the wide range of usefulness of this product in many conditions where a restricted diet is advisable, and particularly in diseases that constitutes a large part of the work of Gastro-enterologists. The purpose, therefore, of the Mellin's Food Company's exhibit is to offer opportunity for free discussion relative to this subject matter, and physicians are cordially invited to call at Booth No 52.

Take a little trip to the birch woods of Connecticut, and see how the Wm S Merrell Company produce the birch oil from which is made their famous Natural Sodium Salicylate.

The Merrell Company are the only pharmaceutical house in the world who produce a Natural Sodium Salicylate from birch oil produced under their own supervision.

At Booth Nos 15 and 16, the Merrell Company will show a small reproduction of one of their Connecticut mills.

The Nelson Loose-Leaf Medicine and the Nelson Loose-Leaf Surgery, each complete in seven volumes with separate Index Volume, will be on exhibition at Booth No 40. These outstanding publications carry with them a semi-annual service consisting of (1) a survey of the medical and surgical literature of all countries, reviewed and annotated by 150 of the foremost physicians and surgeons of America, (2) new and revised articles issued under the direction of the Nelson Advisory Board, (3) a special research service free to all subscribers. To quote the U S Naval Medical Bulletin: "The list of contributors is practically an honor roll of the surgeons of today." Other Nelson medical publications will also be on exhibition.

**SANBORN ELECTROCARDIOGRAPH**  
—For testing at office and hospital, or at

patient's homes, Simplified and accurate—easy for technician or nurse to operate

**SANBORN METABOLISM**—For clinical diagnosis—the GRAFIC, for specialist and research—the SANBORN BENEDICT with its electric blower circulation

At Booth No 54, see the SANBORN ELECTROCARDIOGRAF, SANBORN GRAFIC and SANBORN BENEDICT and DEMONSTRATIONS

W B Saunders Company will exhibit all of their three hundred or more titles, outstanding among these are Beckman's new work on Treatment, Blumer's Bedside Diagnosis, Christopher's Minor Surgery, Campbell's Orthopedic Surgery, Ewart A Graham's new three volume work on Surgical Diagnosis, Cecil's Medicine, Bethea's Medicine Medical Clinics of North America and the Surgical Clinics of North America, Granger's Physical Therapeutic Technic, Norris and Landis Diagnosis by Chest Diseases

Booth No 10—Spencer Lens Company of Buffalo, New York—Exhibit of Microscopes and Accessories, Colorimeters, Retractable Microtomes, Dark Field Illuminators, Lantern Slide, Film Slide, and Opaque Projectors and introducing the SPENCER SYSTEM OF VISUAL EDUCATION Many other things of interest to the Physician and Clinician will be shown "

A physiologically tested vitamin—containing sugar (Vitavose), irradiated ergosterol (Viosterol) products, and a physiologically tested ovarian hormone product will be among the items of interest at the Squibb Booth, No 56 A competent staff of representatives will be present to answer inquiries about these, and other new Squibb Products

Interest in Bacteriophage will undoubtedly draw many physicians to Booth No 28, where members of the scientific staff of Swan-Myers Company will furnish information and literature on this new development in biological therapy The Swan-Myers laboratories were the first to be licensed by the United States Government for the manufacture of Bacteriophage and are at present the only laboratory in the

country to supply Bacteriophage products commercially

Swan-Myers will also have interesting displays of Ephedrine Products, including Swan-Myers Inhalant, No 66, Swan-Myers Pollen Extracts, and Para-Psyllia, Swan-Myers, a new mechanical laxative that combines psyllium seed jelly and mineral oil in a pleasing emulsion

**BIG COD FROM NORWAY**—During the fishing season of 1928, a cod of record proportions was taken from the Lofoten waters of Norway for Nason & Co, the Norwegian subsidiary of Tailby-Nason Co This splendid fish, 4 ft 11 in long and weighing 30 kilos, will form an interesting part of the exhibit of Nason's Palatable Cod Liver Oil, "The Better Tasting Kind," produced in Nason's plants in Norway, at Booth No 60

An announcement of new developments and apparatus will be made at the Exposition of the American College of Physicians, by the Taylor Instrument Companies, Rochester, New York, at Booth No 27

Our representatives who will attend the coming Exposition will be men competent to demonstrate and discuss the technique of operation of our instruments and their value in service

We will be very glad to have members of the American College of Physicians come to our exhibit and investigate our products without any obligation other than to give us an opportunity to present reasons for development and service value of the instruments

"The Story of Foxglove Farm," told in three minutes in movie form, is of major interest to physicians Digitalis is one of the five most important drugs—its potency may be a matter of life or death to the patient Every physician should know the processes and precautions necessary for the production of potent digitalis It is a drug he cannot afford to take a chance on It will be worth while to visit Booth No 45 where the film will be shown by James Upsher Smith of the Upsher Smith Company

The Victor X Ray Corporation will demonstrate, at Booth Nos 61, 62, 63, 64, 75, 76, 77 and 78, its Model "A" Shock Proof

X-Ray Unit which, in addition to being 100% electrically safe, presents many original control features, such as calibrated auto-transformer control, Victor-Kearsley Stabilizer and voltage compensator, which permit a simplified standardized technic hitherto unattainable. There will also be exhibited a comprehensive collection of radiographs made with this Unit.

William Wood and Company, of New York, now celebrating their 126th year as medical publishers, will welcome old and

new friends at Booth No. 24, and exhibit specimen copies of about two hundred of their publications, including many new books and such famous standard works as Bailey—Histology, Bailey and Miller—Embryology, Cabot—Physical Diagnosis, Cunningham—Anatomy, Chapin and Royster—Diseases of Children, Chetwood—Urology, Mathews—Physiological Chemistry, Stedman's Medical Dictionary, and of course the indispensable French—Index of Differential Diagnosis.



# Minneapolis As a Medical Center

By S MARX WHITE, M D , *Minneapolis, Minnesota*

**M**INNEAPOLIS as a medical center is among the newer points in the New World. Its attractions are shared with those of its twin city, St. Paul. The population of Minneapolis in 1930 is over 500,000, and together with St. Paul and the immediate suburbs of both, the metropolitan area lays valid claim to nearly a million people.

The first hospital in Minneapolis was founded in 1871, 120 years after the foundation of the Pennsylvania Hospital in Philadelphia in 1751, which lays claim to be the oldest institution of this kind in this country. This was also exactly 100 years after a Royal Charter was granted in 1771 to "The Society of the Hospital in the City of New York in America." This was the second hospital within the present limits of the Union if we except that in Manila, Philippine Islands, acquired by conquest and not a product of our normal national growth.

The history of Medicine in Minnesota has been determined by the social conditions and has paralleled the rapid growth. The freedom from tradition and the rise of medical service and medical education in this western metropolis exemplifies the development in the social and economic life.

Dr. Richard Odling Budd, who has done a great service in collecting and

recording the facts of this recent history, and to whom the writer hereby acknowledges his debt, shows that following the period of the Preceptor the period of the Private Medical College in Minnesota began parallel with that of the foundation of the first hospital in 1871 in the organization of "The St. Paul Medical School, Preparatory, for Medical Instruction."

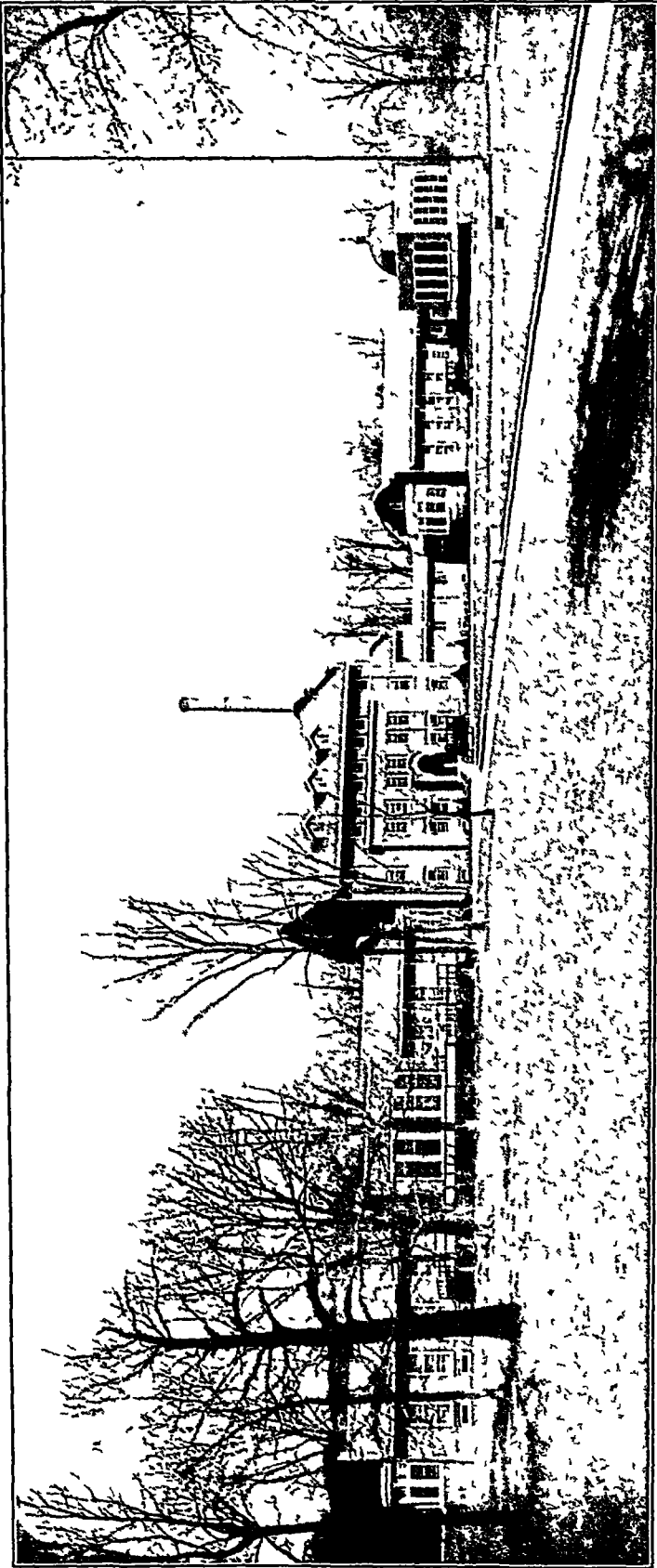
For three years before this, however, students who were "reading medicine" in the doctors' offices in St. Paul had been meeting in a little room perhaps a dozen feet square in the second story of a little stone dead-house where occasionally an amputated limb was dissected, and they were at odd times met and quizzed by preceptors.

This "Medical School Preparatory" had a corps of 8 teachers, a course of 4 months' study, and was designed to prepare students for a better understanding of the lectures to be heard later in medical college. The arrangement of terms of study was such that "they would not interfere with the winter course of the Chicago Colleges."

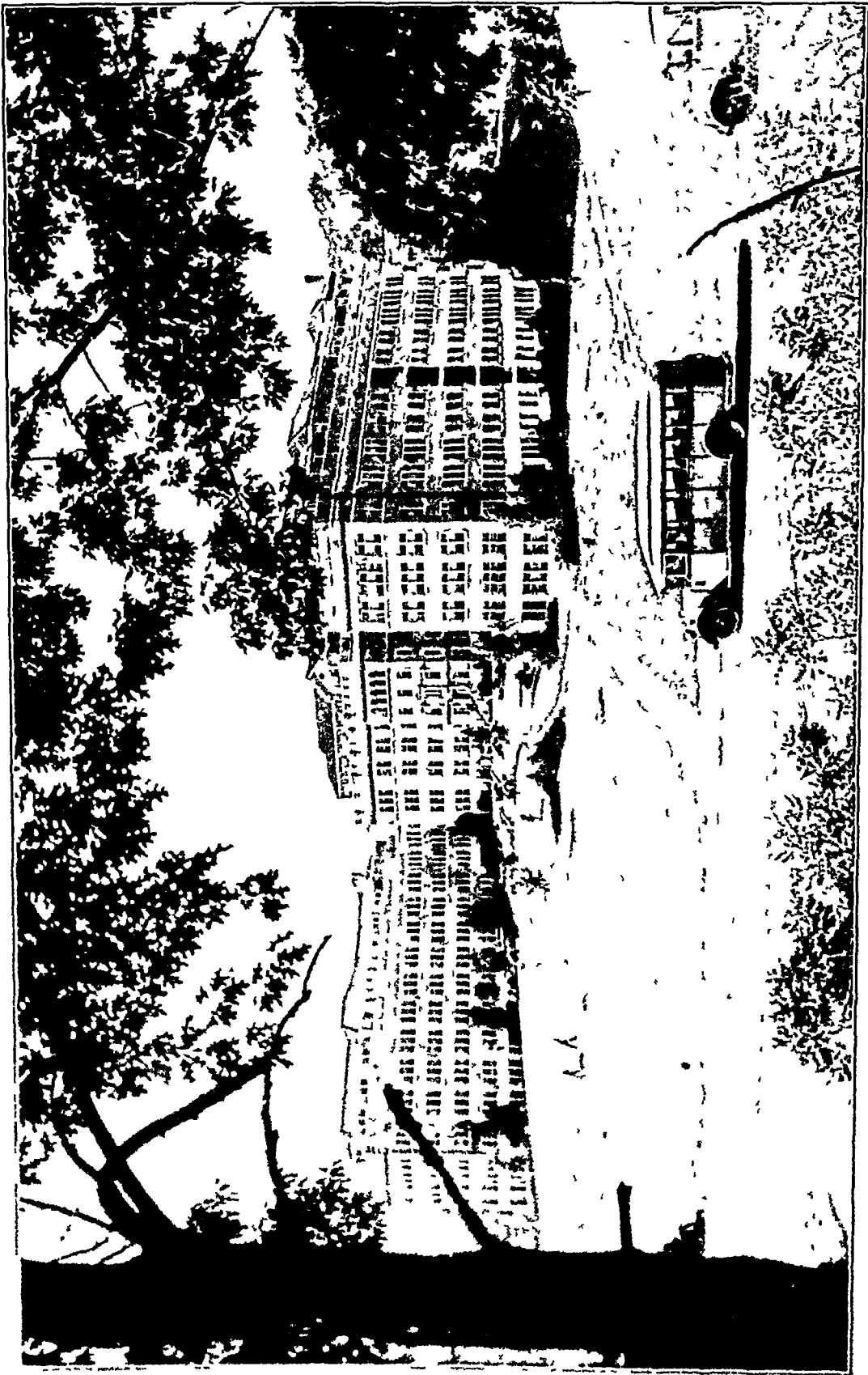
Another private school, the Winona Medical School Preparatory, was begun in Winona, Minnesota, in 1872. They neither granted degrees nor conferred diplomas. They had no Alum-







SHRINERS HOSPITAL  
Minneapolis, Minn



GLEN LAKE SANATORIUM  
Minneapolis, Minn

The St Paul Medical College was organized as the Medical Department of Hamline University in 1878 and closed with the spring session of 1881. Its Faculty combined with additional physicians of St Paul and physicians of Minneapolis to found the Minnesota College Hospital in the last named city. It is said that the élite of St Paul and Minneapolis gathered on the 31st day of October, 1881, in the elegantly fitted lecture room of the College to witness the opening of the school. The first Commencement exercises were held on March 24th, 1882.

In 1883 the University created the Department of Medicine of the University of Minnesota, its Faculty being

a non-teaching and purely examining body. This body during a brief period served as an educational influence felt in the medical schools of Minnesota and of other states as evidenced by the qualifications required of candidates for the state examinations and quoted by Dr. Beard as follows:

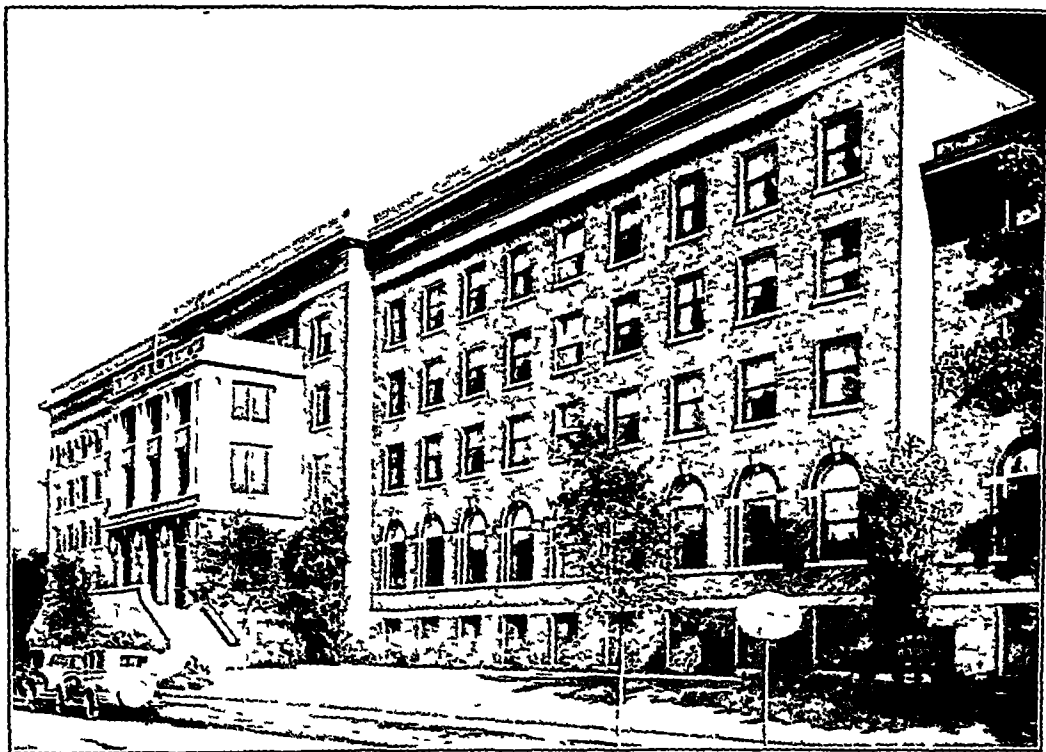
1 Attendance upon one full course of lectures upon the subject of each study under examination.

2 A familiarity with the literature of the subject.

3 Clinical and laboratory experience.

4 Skill in the actual use of physical and chemical tests in diagnosis, etc.

5 A certificate of dissections of the



NEW ASBURY HOSPITAL  
916 E 15th St  
Minneapolis, Minn

muscular, nervous, and circulatory systems

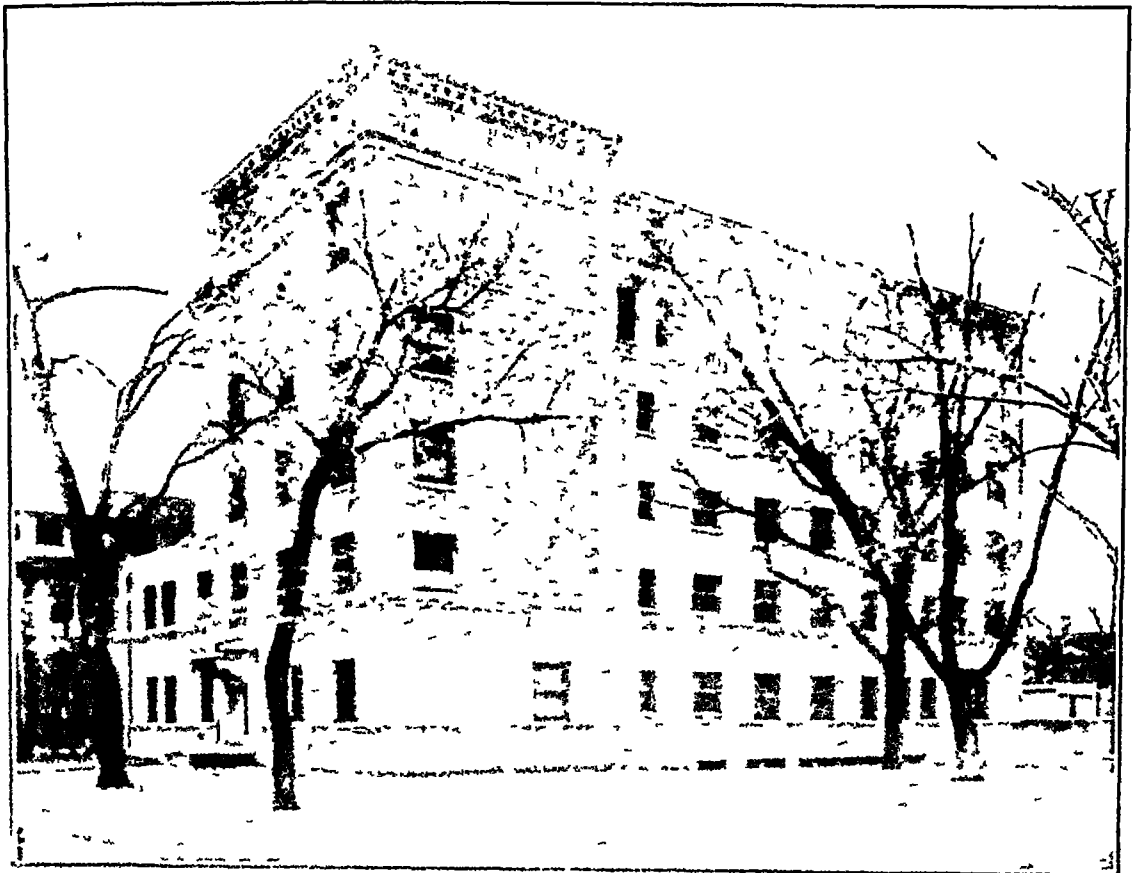
In the subjects for examination are named, as prerequisites in Physiology, the demonstration of normal tissues and products and the relation of the living body to its environments, in Pathology, the demonstration of specimens and examination of cases for diagnosis and the use of chemical agents and the microscope to this end, under Practice, the use of diagnostic instruments and a systematic examination and record of cases

In 1883 another new college was created under the name of the Minneapolis College of Physicians and Surgeons which, in 1895, was adopted by Hamline University as its Department

of Medicine and continued so until its fusion with the Medical School of the University of Minnesota in 1908

During the earlier years this School granted no degrees, but referred its students to the Department of Medicine of the State University for examination, it being remembered that this Department of Medicine was then purely an examining body

Meanwhile the Minnesota Hospital continued its courses and during the session of 1884-5 a unique announcement was made by its Dean that "Dr John F Fulton, Professor of Ophthalmology and Otolaryngology will give a free clinic on diseases of the eye and ear at the College building upon each Friday All indigent afflicted are in-



ST. ANDREW'S HOSPITAL.

vited to avail themselves of the attention now, for the first time in the history of our State, offered to them"

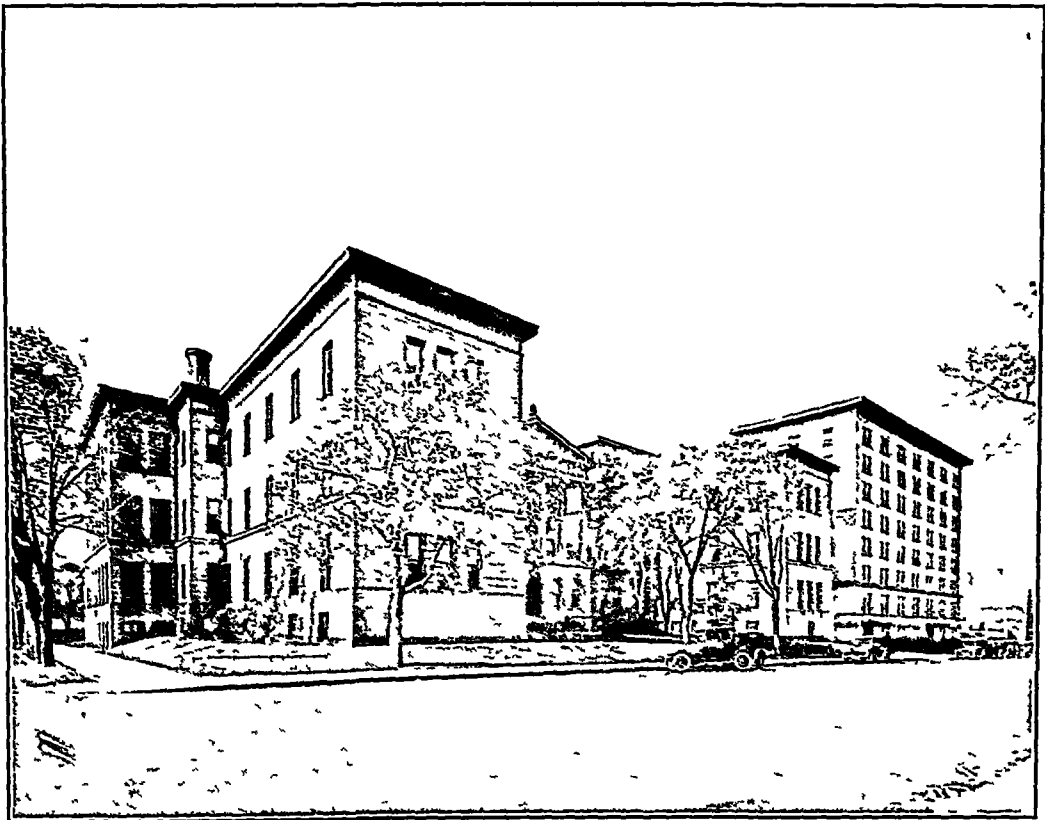
Dr Fulton is living and active, an honored citizen of St Paul today

In 1885 the St Paul members of the Faculty of the Minnesota College Hospital resigned and the name was changed to the Minnesota Hospital College, moving to a new building in September, 1886 The St Paul members of the Faculty reorganized the St Paul Medical College which opened in the fall of 1885 and likewise dedicated a new building in 1886

In October, 1886, the Minnesota Homeopathic Medical College was organized and lasted for two years with

a faculty of 16 and students numbering 20

In 1887 an independent State Board of Medical Examiners was created by the Legislature With the single exception of an antiquated measure in South Carolina, this was the first Act of its type upon the statute books of any state and the Act since that day has been the model of most of the Medical Practice Acts in the United States In the same year the Board of Regents of the University of Minnesota was petitioned to establish a teaching Department of Medicine of high grade in the University, and the Legislature was asked to provide for its maintenance In February, 1888,



MINNEAPOLIS GENERAL HOSPITAL



the faculties of the Minnesota Hospital College and the St Paul Medical College offered to surrender to the Board of Regents their charters and tendered their properties for the temporary use of the State, and a month later the Minnesota College of Homeopathic Medicine did likewise

The proposals were accepted by the Regents and faculties were named and organized for the Colleges of Medicine and Surgery and of Homeopathic Medicine and Surgery Later, Colleges of Dentistry and Pharmacy were added

Thus, in October, 1888, the first entrance examinations were held and systematic instruction begun in a

course of study covering three years of six months each

In 1890 the Medical College term was lengthened to eight months

In 1893 the Legislature provided for the removal of the Department of Medicine to the University Campus and with that Act University instruction in Medicine in Minnesota may be said to have received its greatest impetus

In 1900-01 entrance examinations to the College of Medicine and Surgery were made identical with those of other departments of the University and some election was provided for in certain special subjects Beginning with the opening session of 1901, the



ST. BARNABAS HOSPITAL, FOUNDED 1871

college year was extended to nine months

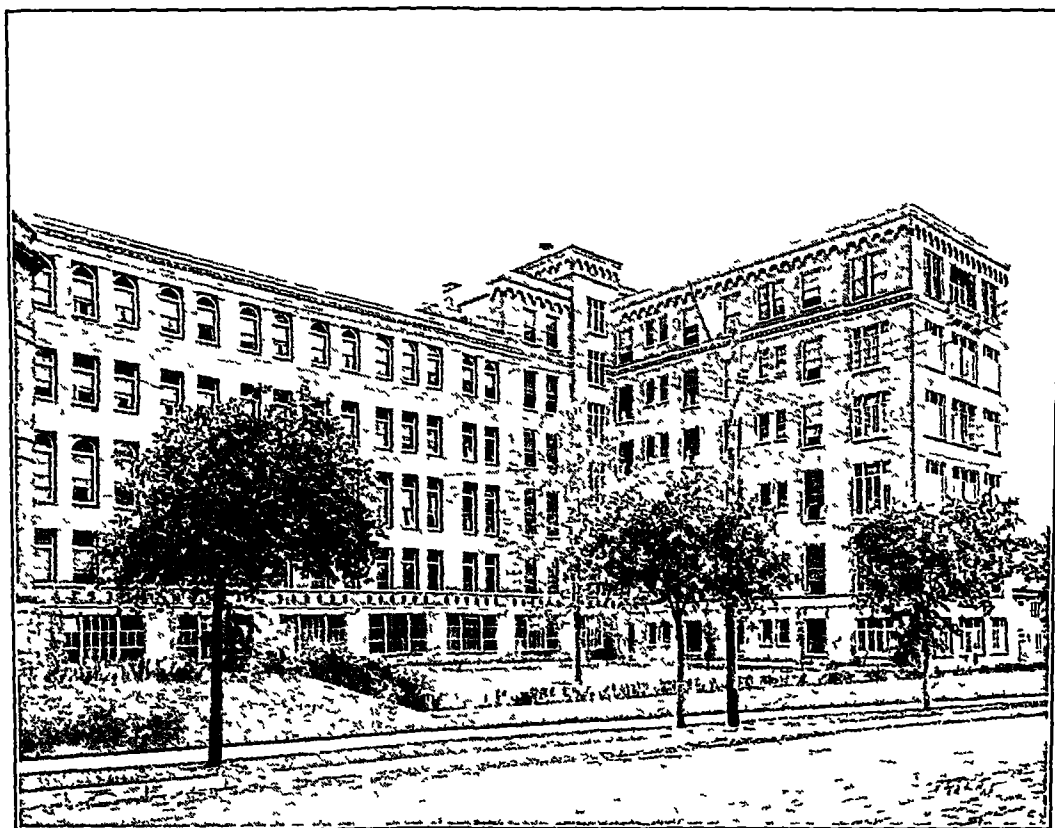
In the fall of 1903 a six-years' course looking to the degrees of B S and M D was begun, the first degree to be conferred at the close of the fourth year, and the latter at the end of the sixth year, the last two years of the course for the Bachelor's degree being given in the Medical School. Later the degree of M B was given at the completion of the required six years, and the degree M D given at the completion of a required year of internship in an approved hospital.

The history of the hospitals of the University of Minnesota begins with the announcement of a bequest from

the estate of Dr and Mrs A. F. Elliott to be devoted to the building of the Elliott Memorial Hospital. This was promptly followed by provision through a group of philanthropic citizens of Minneapolis for the purchase of a hospital site.

In 1906, Dr. Frank Fairchild Westbrook, who had come in 1896 as Professor of Pathology and Bacteriology and was Director of the Laboratories of the State Board of Health, was made Dean of the Medical School and became the moving spirit in a period of unprecedented development in medical education in Minnesota.

In 1906 a plan was adopted by which all medical education in Minne-



NORTHWESTERN HOSPITAL  
Minneapolis, Minn

sota should be unified in the University. The Medical School of Hamline University was discontinued and certain members of that Faculty were invited to positions on the University teaching corps. The School of Homeopathic Medicine and Surgery of the University survived but a little time longer.

The development of the University Hospitals, begun with the Elliott Memorial unit, has been slow but continuous. The Todd Memorial and the Cancer Institute increased greatly the teaching facilities, and the year 1929 has witnessed the completion of the Eustis Memorial and the hospital of

the Students' Health Service, together with the transfer of the Out-Patient Department to the University Hospital group of buildings.

To attempt to cover in detail all the progress of the past twenty years would be tiresome and is at this point unnecessary. A great Medical School is in full operation. An important medical center is established and serves a far-flung territory. The cities of Minneapolis and St. Paul, by the keenness of their rivalry, are compelled to an adoption of the most modern facilities. The proximity of the unique and world-famous Clinic and Mayo Foundation at Rochester, less than 100



NEW \$700,000 SWEDISH HOSPITAL BLDG  
10th Ave So. & 8th St  
Minneapolis, Minn

miles away, provides an additional stimulus

In addition to under-graduate instruction, an important type of graduate instruction in Medicine has been established, functioning for the Medical School and for the Mayo Foundation, under the Graduate School of the University of Minnesota

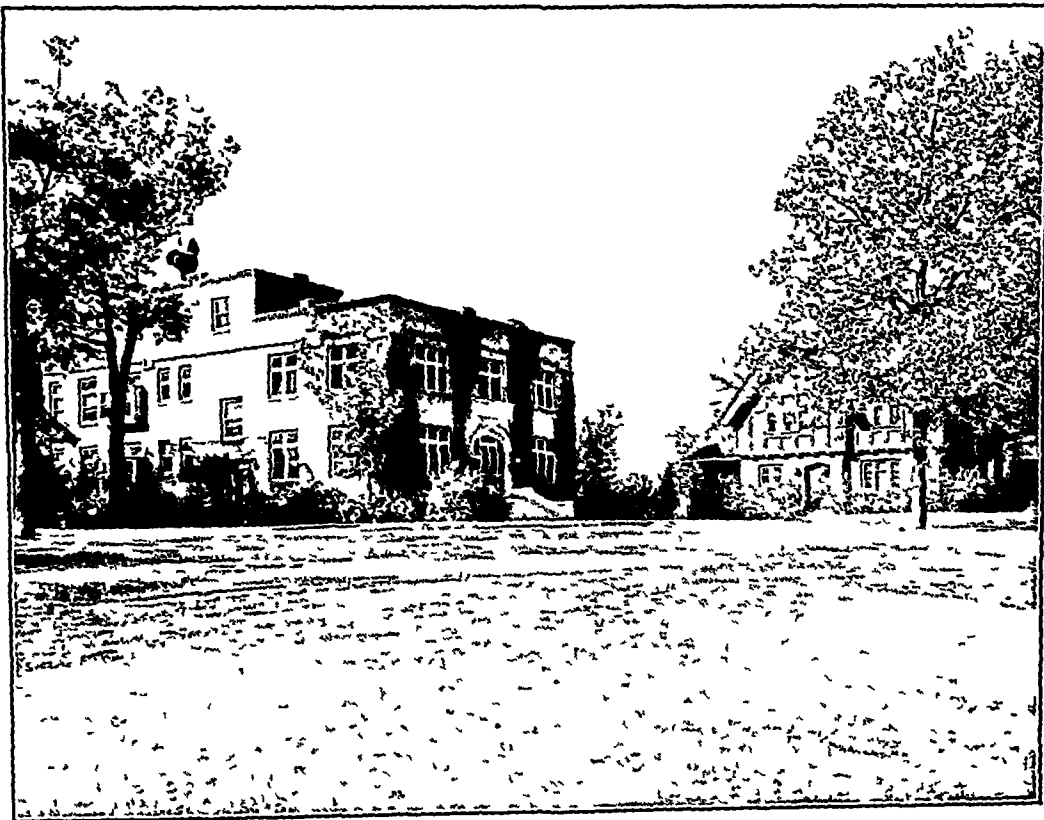
Candidates for the higher degree of M S and Ph D in the various departments of Medicine, Surgery, and the Medical Sciences take their work either in the Medical School in Minneapolis or at the Mayo Foundation in Rochester

The pursuit of true graduate study by a rapidly growing number of men

and women has had a profound effect upon the character of teaching in the Medical School and has been a large factor in the constantly increasing contributions to knowledge in Medicine

When Dr Westbrook was chosen to head the University of British Columbia in 1913, Elias P Lyon was chosen his successor as Dean

The first step by the University providing arrangements by which heads of clinical departments devote their entire time to teaching and investigation was taken in 1915 when Dr L G Rowntree was appointed to head the Department of Medicine. Provision was agreed upon by which a small hospital should be arranged for his private



MATERNITY HOSPITAL, Inc  
2215 Glenwood Ave  
Minneapolis, Minn

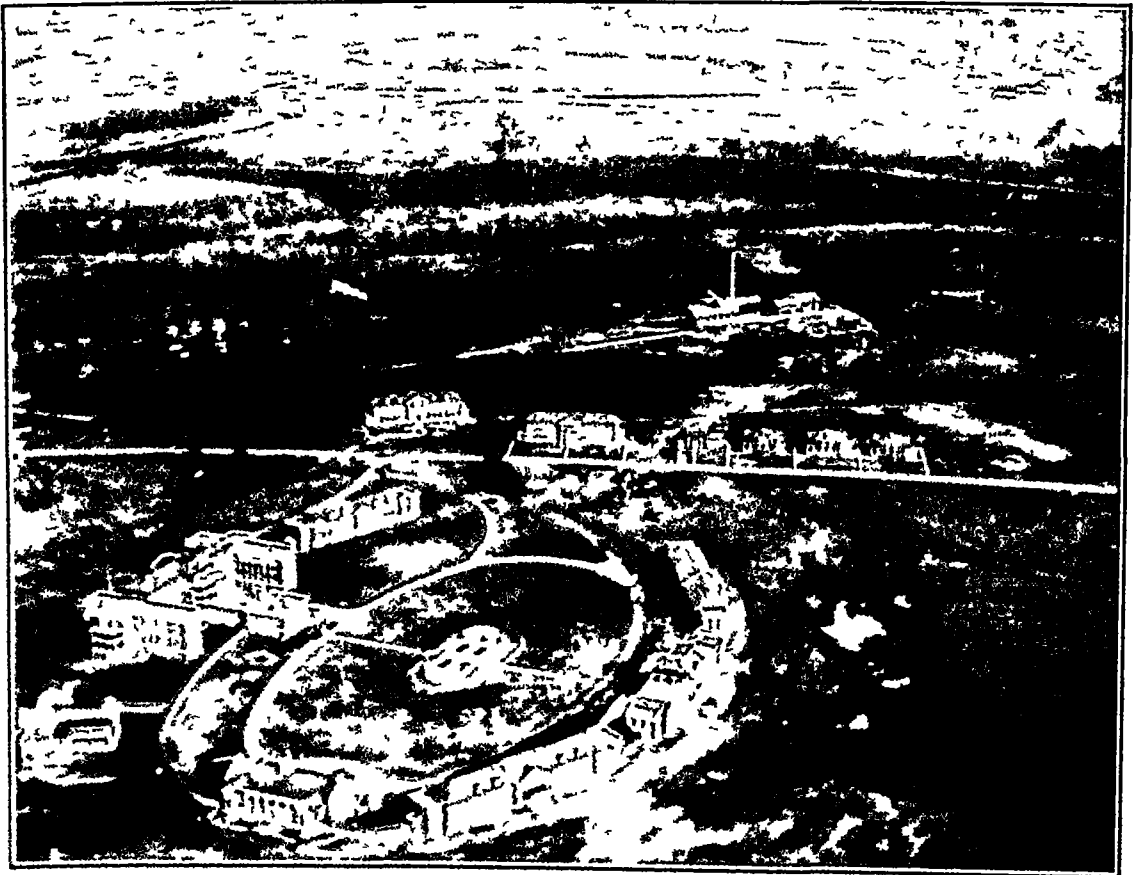
patients in one of the houses on the Campus. The latter part of the arrangement was never carried out but he was given space for an office in one of the buildings of the Medical School and was allowed to see patients there as long as he remained. This arrangement terminated in 1920 with his removal to the Mayo Foundation in Rochester.

In 1918 the late Dr. Julius Parker Sedgwick gave up his private practice in Pediatrics and became a full-time Professor with the privilege of consultation.

With these beginnings the principle of full-time heads of departments and

of increasing full-time employment on the part of University clinical teachers has been growing as opportunity was afforded and, with the exception of the Departments of Obstetrics and Gynecology and of Ophthalmology and Otolaryngology, the clinical Departments now have full-time teachers in charge.

The system under which they work is known as the Harvard System and may be characterized as "geographical full-time", the latter expression meaning that all of the teacher's work is done in one place. He does not maintain an outside office, he is not affiliated with any outside group, nor is he on the active staff of any private hos-



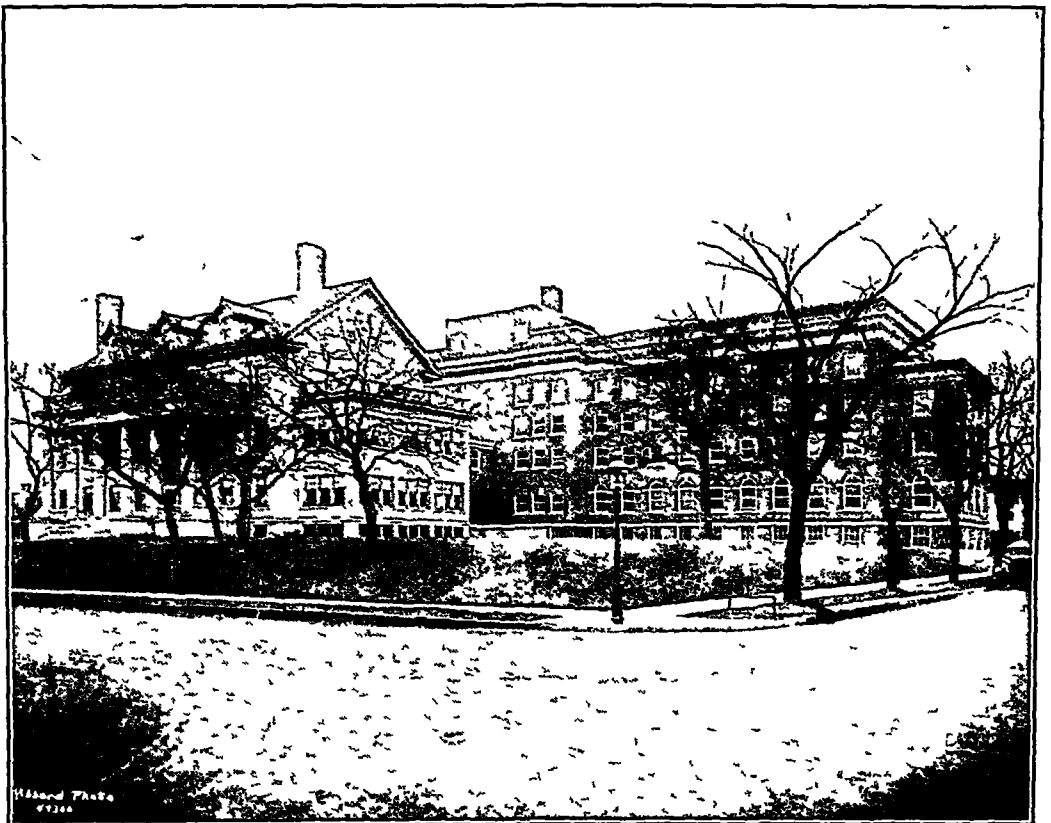
AERIAL VIEW OF UNITED STATES HOSPITAL NO. 100  
This Hospital is located on the Banks of the Mississippi just outside of the West City  
Limits of Minneapolis and on the Fort Snelling Military Reservation

pital, his outside work is limited to consultation with other members of the Medical Profession, and in general the full-time members of the Medical School Faculty conform with the regulations for outside work as outlined in the rules and regulations of the University of Minnesota governing all the departments of the institution. This system is virtually that in use at Harvard, Columbia, in partial use at the University of Iowa and in some others.

The hospitals of Minneapolis provide the housing for this most significant type of medical service. The University Hospitals comprise the Elliott Memorial, the Todd Memorial, the Cancer Institute, the Eustis Memorial,

and the Hospital for the Students' Health Service, with a total of 480 beds. The buildings house also the Out-patient Department of the Medical School. The Hospital is located on a commanding site overlooking the gorge of the Mississippi and the buildings of the Medical School and of the Departments of Biology of the University are close by.

The Minneapolis General Hospital is a tax-supported institution, receives some partial payment of per diem costs from patients sufficiently able to pay, and has 474 beds, of which 386 are general and 88 in the contagious pavilion. It is located at 5th Street and 7th Avenue South, within nine



THE TOURTELLOTTE MEMORIAL DEACONESS HOME AND THE  
NEW ASBURY HOSPITAL

blocks of the Auditorium Connected with it, but in the outskirts of Minneapolis, is the Parkview Sanatorium for chronic patients, with 140 beds A large voluntary service staff is selected from physicians of the City and University Faculty One member of the Faculty is on full-time and two on part-time paid service There are 3 Teaching Fellows, 8 chief Residents, and 24 Interns on the professional house staff

Of the private and semi-private hospitals, St Barnabas is the oldest It was founded in 1871 and was the hospital referred to in the second paragraph of this article It is situated at

901 South Sixth Street, is a general hospital, and has 170 beds

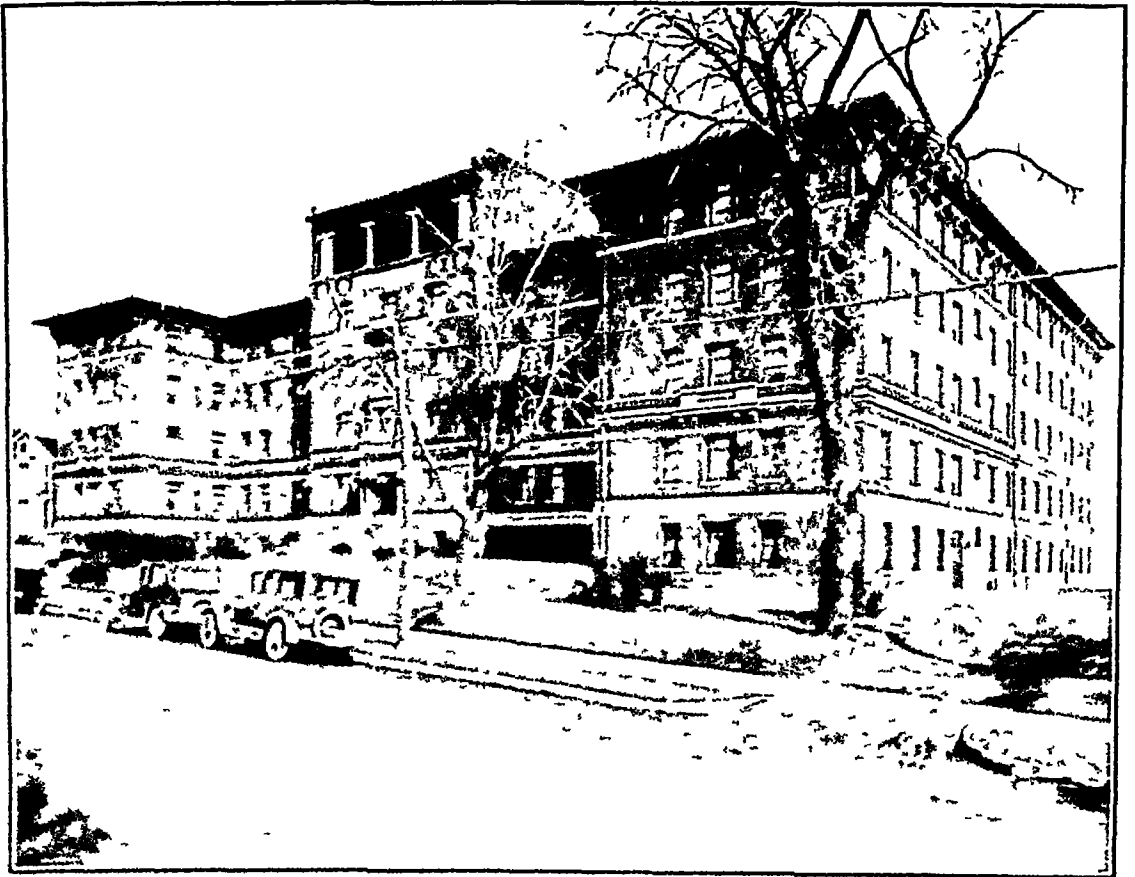
Abbott Hospital is located at 1717 First Avenue South, is a general hospital with a large children's pavilion, and has a total of 100 beds

The New Asbury Hospital is located at 915 East 15th Street, is a general hospital, and has 140 beds

Eitel Hospital is located at 14th and Willow Streets facing Loring Park, and has 130 beds

Fairview Hospital, at 2316 Sixth Street South, is a general hospital, with 200 beds

Hillcrest Surgical Hospital at 501 Franklin Avenue West, has 75 beds



FAIRVIEW HOSPITAL  
Minneapolis, Minn

The Lutheran Deaconess Hospital, 1412 East 24th Street, is a general hospital, and has 150 beds

Maternity Hospital, at 2215 Western Avenue, is obstetrical and pediatric, and has 100 beds

Northwestern Hospital, 2627 Chicago Avenue, covers the fields of medicine, surgery and pediatrics, and has 200 beds

St Andrews Hospital, 712 Fifth Street S E, provides general service, and has 100 beds

St Mary's Hospital, 2500 South Sixth Street, is a general hospital, with 250 beds

The Shriners' Hospital for Crippled Children, one of eleven hospital units distributed throughout the country, is located at 2025 East River Road, and has 62 hospital beds

The Swedish Hospital at 723 Tenth Avenue South, has just completed and dedicated a new building. It provides general service and has a total capacity at present of 322 beds

Thomas Hospital is a hospital for tuberculosis, with 65 beds, and is situated at 2340 Sixth Street South

Glen Lake Sanatorium, which is the sanatorium for tuberculosis for Hennepin County, is in a suburb of Minne-



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United States Veterans Hospital No 106 is located at Fort Snelling, about 7 miles from the Auditorium, is a general and tuberculosis hospital and has a normal capacity of 469 beds, with a maximum capacity of 541 beds

The hospitals briefly mentioned here are shown in the photographs accompanying this article

The total hospital capacity of Minneapolis, when only its active general beds are included is, therefore, 2891 When the United States Veterans Hospital, Glen Lake Sanatorium, with Parkview, Shriners, and Thomas hos-

pitals, i e , the more chronic and special forms of hospitalization and sanatorium care in and about this medical center, are counted, their beds number 1436, the total of all forms of hospital beds being, therefore, 4327

The value of any group functioning as a center lies, however, not in the character of the buildings nor in the excellence of the equipment These are necessary in order that provision be made for modern types of work, and the background of history and the details of physical equipment have been sketched only that an idea may be formed as to the status of economic development



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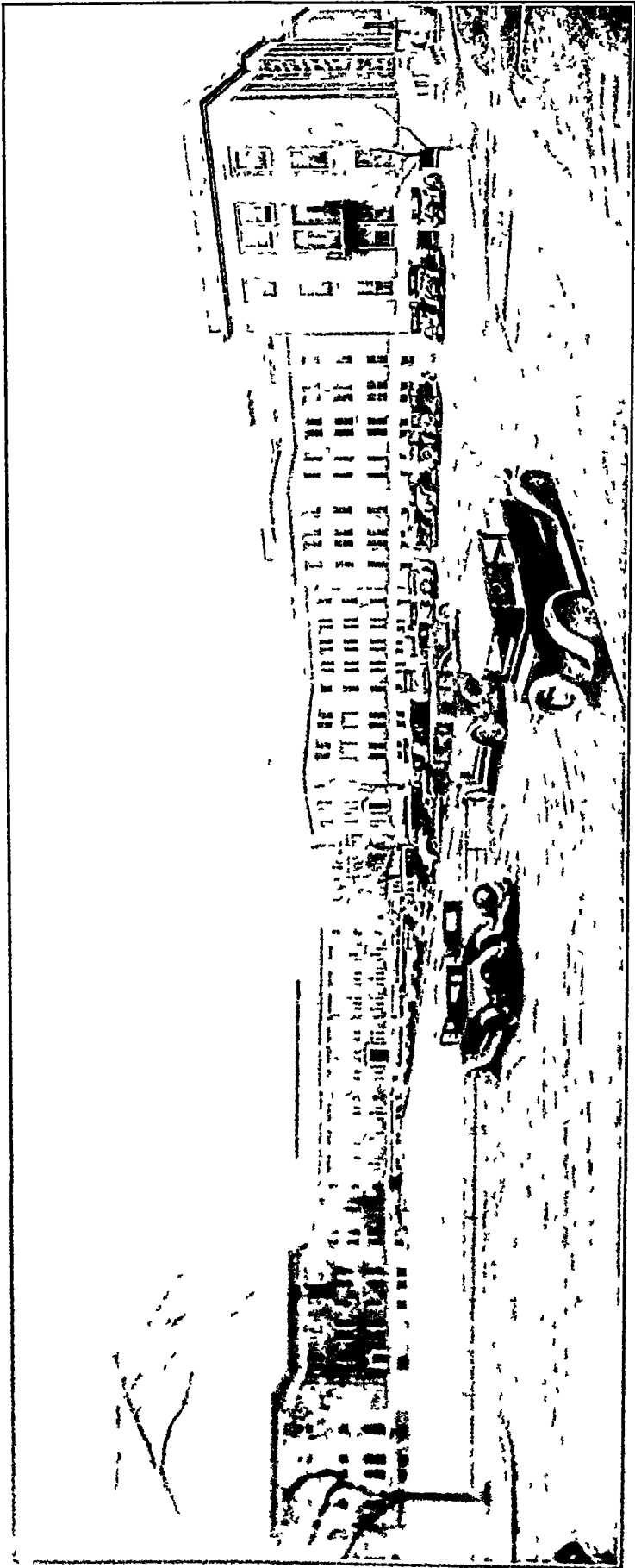
The spirit of the men whose lives have gone into the making can be caught only by long and searching study. There are those whose time, in part at least, is now being given to attempts to put into the record before it is too late something of the lives of

these men, the very mention of whose names has been impossible.

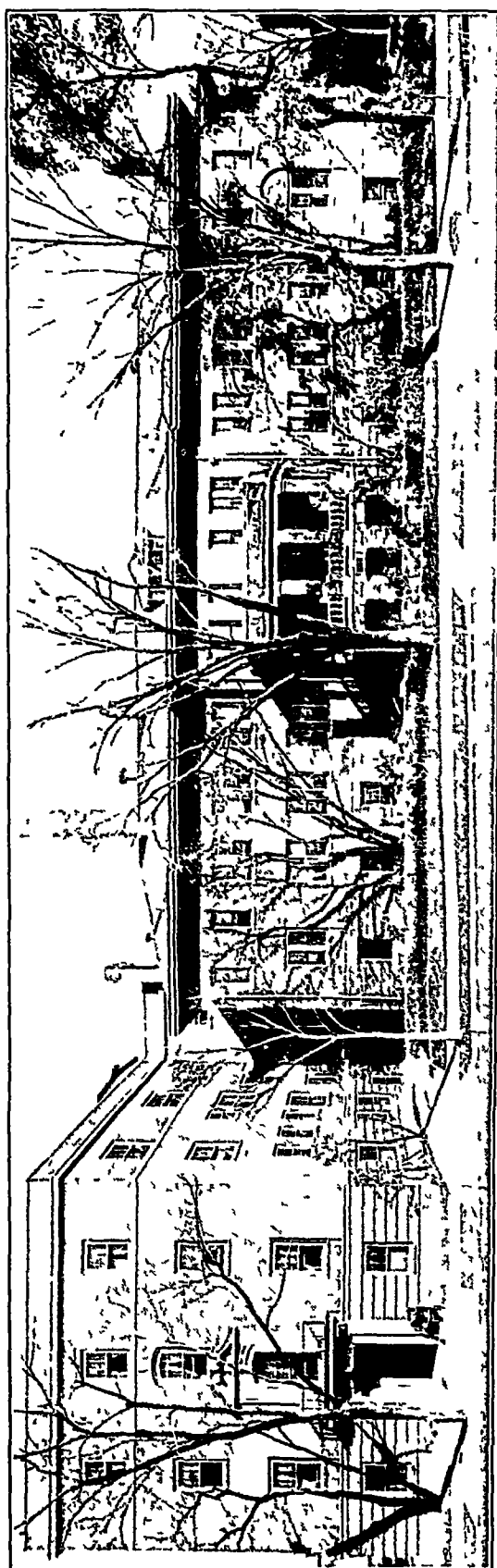
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What arrangements for illustration do you desire for the paper you are to present at the Minneapolis session the week of February 10?

A lantern will be provided for the standard size lantern slides. If x-ray films are to be shown in illuminating box, we should know that and have proper preparation made. If you are to present moving picture films and are bringing your own projection apparatus, we should know that and have provision made for the kind of current you desire. If we will need to provide projection apparatus for moving picture films we must know the size of the films to be shown.

In a word, if apparatus of any kind is needed in the presentation of your paper, we must have before January 15th a full description or statement of all the material to be provided by the local committee. Technical details should be furnished wherever necessary.

Another matter of importance which concerns each essayist relates to newspaper publicity during the meeting. I am aware that most of us desire in every way to avoid any newspaper publicity and will do anything to prevent it. It is just as clear, however, that the meeting of The College is one of importance and the public has a right to know what is going on in our profession.

The Hennepin County Medical Society has a committee on publicity which has been functioning effectively for some time and

is co-operating with our committee for this meeting. One of the purposes of the committee is to get before the public in proper form information for those capable of giving it, and the coming meeting will afford an opportunity for the exercise of this function. The committee proposes to see that medical information is given to the press in dignified and proper form, knowing that if this is not done, the press will secure its own information and that the form in which it is published is usually, as we view it, extremely ineffective and does not bring out the greatest values in our work in medicine.

You may feel that your particular paper has no interest for the general public, but it happens that the newspaper and not we will make this decision. In order that the committee may be prepared to aid the press in the proper interpretation and news presentation of the addresses, our committee is asking that you furnish the committee on publicity with an abstract of your paper, or if it is ready by that time, a copy of the manuscript. The purpose of this is that the members of the committee on publicity may be informed in advance and prepared to aid the press in evaluating your material and bringing out of it the greatest values to the public.

The abstract or manuscript should reach us by January 15 at the latest and should be addressed to Dr. J. A. Myers, Chairman, Committee on Publicity, 730 La Salle Building, Minneapolis.

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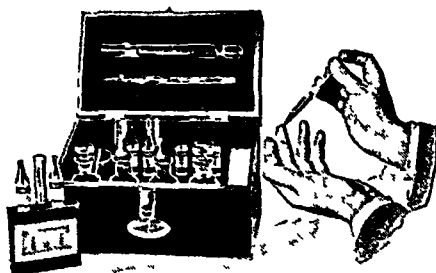
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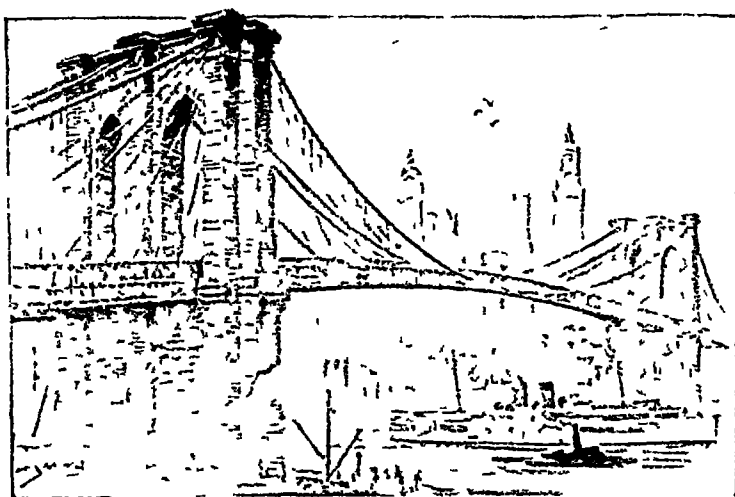
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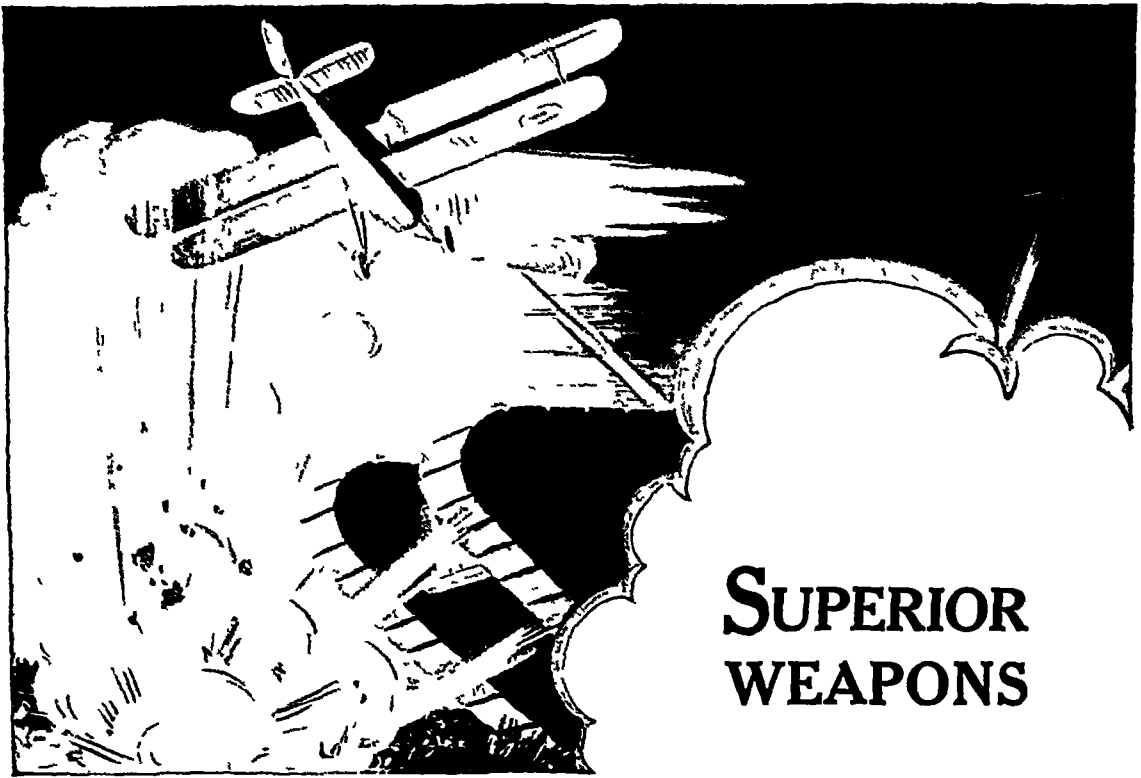
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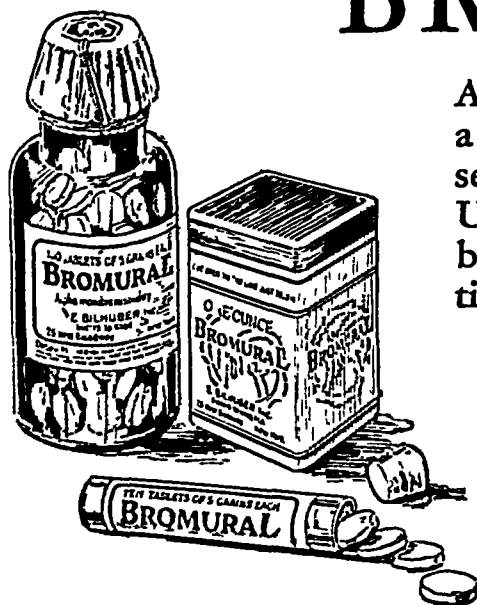


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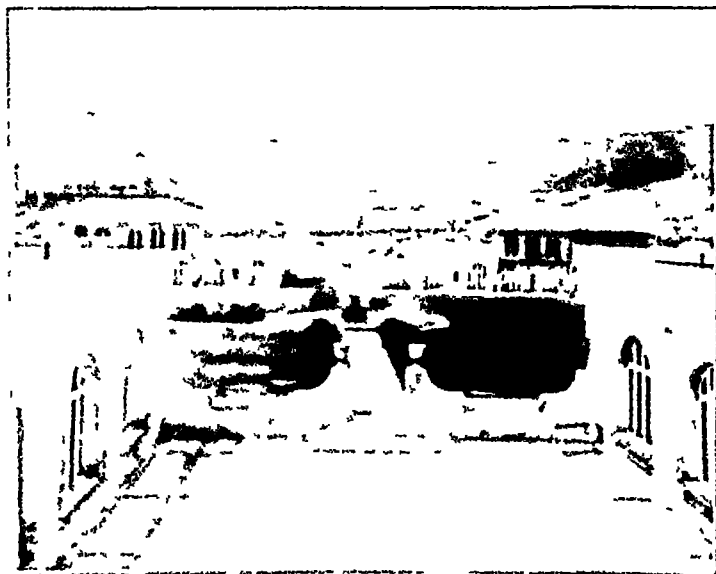
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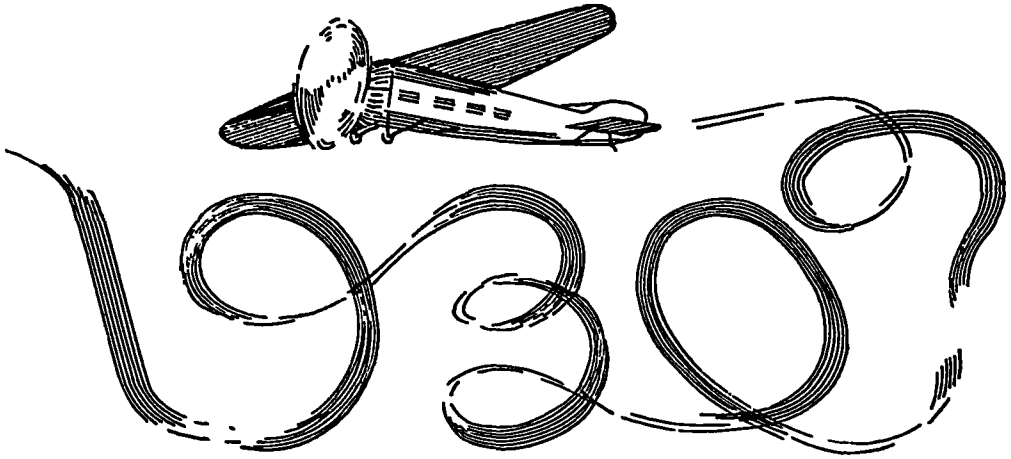


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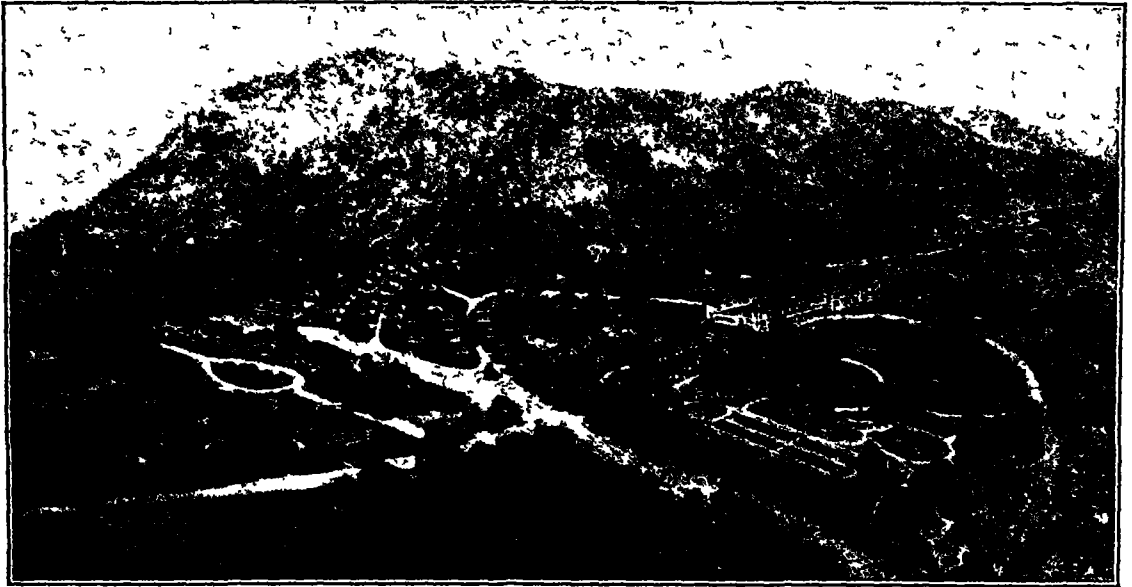
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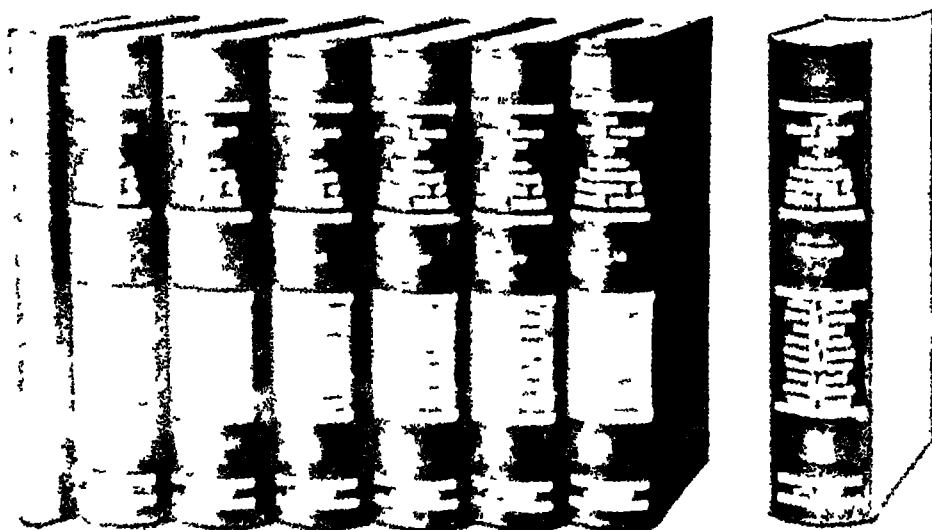
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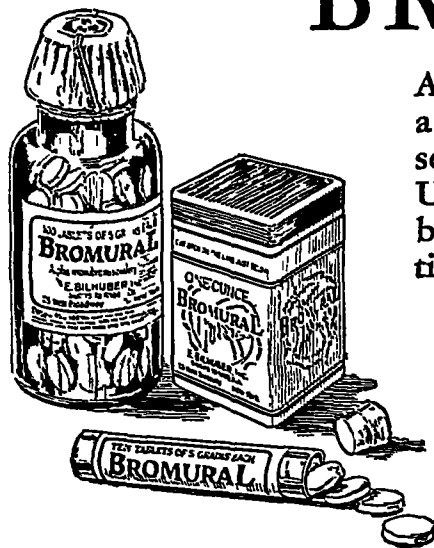
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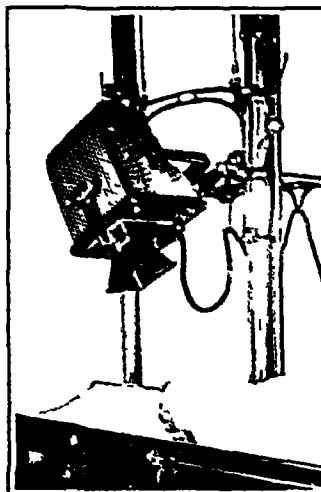
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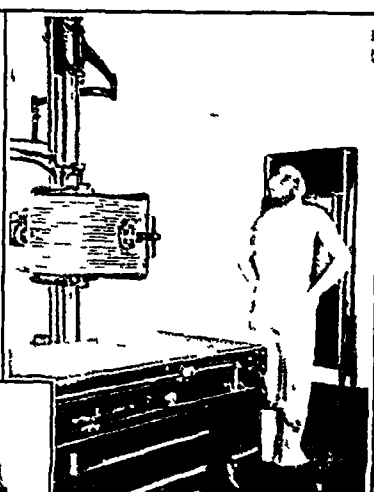
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# The Lactic Acid Content of the Blood and the Partition of Inorganic Sulphate in the Serum of Patients With Hepatic Disease\*

By E G WAKERFIELD, M D *Fellow in Medicine, The Mayo Foundation, and*  
CARL H GREENE, M D, *Division of Medicine, the Mayo Clinic*  
*Rochester, Minnesota*

THE majority of tests for hepatic function in clinical use at the present time are concerned primarily with disturbances in the formation and excretion of bile<sup>11</sup>. Disturbances in the metabolic activity of the liver, on the other hand, are much less readily demonstrated in cases of hepatic disease. Significant disturbances in the level of blood sugar that can be ascribed solely to hepatic insufficiency, are exceedingly rare. Our experience with both fructose and galactose tolerance tests has indicated that although positive tests occur with greater frequency in the presence of hepatic disease, yet so many other factors influence the response to sugar tolerance tests, and the individual variations are so great, that such tests are of little diagnostic value in any individual patient.

Experimental work on animals has amply demonstrated the rôle of the liver in the catabolism of the amino acids and the formation of urea. The blood urea in cases of jaundice tends to fall within the lower limits of nor-

mal but is not sufficiently lowered, of itself, to be of diagnostic significance. Other factors besides hepatic insufficiency probably are responsible for this reduction in the blood urea. Certainly the occasional development of uremia in cases in which the liver is injured indicates that ureogenesis is still active.

Various other tests, among them the study of the level of lactic acid in the blood, and of the rate of disappearance from the blood of intravenously injected solutions of sodium lactate, have been suggested as tests for hepatic insufficiency. Several investigators, including Schumacher and Adler and Lange have reported that in cases of cholecystitis or cholelithiasis, or in cases of mild catarrhal jaundice, the concentration of lactic acid in the blood was normal, whereas in cases of acute yellow atrophy, carcinoma with extensive metastasis to the liver, cholangitis, advanced cirrhosis or in other types of marked hepatic disturbance, they found that the concentration of lactic acid in the blood was increased. Beckmann, and Beckmann and Mirsalis, on the other hand con-

\*Submitted for publication September 6, 1929



## CHEMICAL CHANGES IN THE BLOOD IN HEPATIC DISEASES

Case	Age	Sex	Serum bilirubin mg for each 100 cc	van den Bergh direct reaction	Blood urea, mg for each 100 cc	Blood sugar, mg for each 100 cc	Lactic acid, mg for each 100 cc	Sulphate parti- tion in serum			Diagnosis
								Total sulphates, mg for each 100 cc	Inorganic sulphates, mg for each 100 cc	Conjugated sulphates, mg for each 100 cc	
1	50	M	12	+	24	76	90	75	45	30	Myocardial failure, chronic passive congestion of liver
2	62	M	08	+	21	91	98	42	30	12	Cholecystitis with stones
3	31	M	15	+	23	100		66	37	29	Cholecystitis
4	52	M	07	0	21	119	79	57	42	15	Cholecystitis
5	42	M	13	+	31	82	113	99	62	37	Stone in common bile duct
6	56	M	43	+	16	93		60	36	24	Cholecystitis with stones, obstructive jaundice
7	52	M	140	+	21	83	90	36	16	30	Obstructive jaundice, stone in common bile duct
8	28	M	41	+	37	110	167	90	60	30	Obstructive jaundice, stone in common bile duct
9	45	M	104	+	25	94	153	48	30	18	Stone in common bile duct
10	61	M	52	+	21	85	81	73	72	01	Obstructive jaundice, stones in common bile duct, severe hepatitis
11	63	M	234	+	19	100	170	75	39	34	Obstructive jaundice, stric- ture of common bile duct
12	38	M	41	0	21	90	120	72	51	21	Obstructive jaundice, stric- ture of common bile duct
13	52	F	54	+	22	78	221	30	30	00	Obstructive jaundice, stric- ture of common bile duct following operation (else- where)
14	44	M	196	+	19	72	93	60	60	00	Obstructive jaundice due to injury to common bile duct at operation (elsewhere)
15	41	F	44	+	12	85	200	34	34	00	Obstructive jaundice, stric- ture of common bile duct*

\*Patient died, diagnosis confirmed at necropsy





blood. Thus, Campbell and Maltby found as great, or greater, increases during the course of fructose tolerance tests, and Meakins and Long reported much more marked changes in cases of circulatory failure. The increases after muscular exercise also emphasize the role of the muscles both in the production of lactic acid and its possible resynthesis to glycogen.

These same factors enter into the interpretation of tolerance tests based on the injection of solutions of sodium lactate. Furthermore, the latter is available commercially only as the racemic salt. Cori and Cori, in particular, have shown that whereas the injection of solution of sodium D-lactate leads to the formation of glycogen in the liver, its optical isomere, sodium L-lactate, forms hardly any hepatic glycogen. The racemic salt, therefore, is obviously unsuitable for use in the testing of hepatic function.

The inorganic sulphate in the serum was slightly increased in nearly 80 per cent of this series of cases, and was greater than 40 mg for each 100 c.c. in thirteen cases of the twenty-six studied. Wakefield has pointed out the variability in the concentration of sulphate in the serum. He found that the values obtained in patients in hospitals who were without apparent renal or hepatic disease were higher than those found in active young normal adults. He also found that the concentration of sulphate in the serum was slightly affected by variations in the urinary output. The intake of fluid apparently was adequate in the present series of cases, and with one exception, case 22, there was no definite renal insufficiency. Many authors, however,

such as Walters and Parham, have emphasized the development of renal insufficiency in jaundice, especially in the terminal stages, and the increase in the content of sulphate in the serum in these cases may be evidence of such renal injury.

The most striking change in the partition of sulphate in the serum in this series of cases was the reduction in the ethereal or conjugated sulphate fraction. The quantity of conjugated sulphates in the serum was 0.5 mg for each 100 c.c. or less, in eleven of the twenty-six cases studied. All the patients with low values were seriously sick, and minimal values were found in the patients who died from hepatic insufficiency.

It is generally accepted that the ethereal sulphate<sup>11</sup> fraction in the urine varies with the amount of intestinal putrefaction. Dietary influences also play a part, for a diet of meat increases, and a diet of carbohydrate decreases, the output. If the level of ethereal sulphate in the blood varies in the same manner as the urinary output, the changes observed may be ascribed either to the special diet of these patients or to the effect of biliary obstruction and the resultant exclusion of bile from the intestine. Biernacki, on the other hand, has described an increase in the excretion of ethereal sulphate in the urine in cases of jaundice. The changes in the level of ethereal sulphate of the serum in this series of cases cannot be wholly explained on this basis, however, for they are apparently more closely related to the severity of the hepatic disease than they are to the presence or absence of biliary obstruction. Although this re-

lationship is very suggestive, yet too little is known regarding the relationship between the physiologic activities of the liver and metabolism of sulphur to permit the dogmatic statement that this reduction in the level of ethereal sulphate in the blood is an index of hepatic insufficiency

#### SUMMARY

A slight increase in the content of lactic acid of samples of blood taken before breakfast was found in some patients with severe hepatic disease

The increase was not sufficiently great, and did not occur with sufficient frequency, to make this test of great diagnostic significance or usefulness

The inorganic sulphates in the serum were increased slightly in the present group of cases, whereas the conjugated or ethereal sulphates were reduced to less than 0.5 mg for each 100 c.c. of serum in patients with severe or terminal hepatic disease. Further study is necessary to determine the diagnostic and prognostic value of this observation

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# Spontaneous Rupture of the Heart; Perforation of the Interventricular Septum\*†

By ALBERT S. HYMAN, M.D., *New York*

**R**UPTURE of the heart is always of serious moment, death is said to follow almost instantaneously. This is especially true of the so-called "spontaneous ruptures" of the heart where the underlying pathology has in most cases been due to a previous disturbance in the circulation of the coronary vessels.

Ruptures of the heart as a result of trauma, gunshot, or penetrating wounds are, however, not necessarily fatal. I have reported the instance of a young negro who was able to run nearly a quarter of a mile with a knife blade sticking through his chest and piercing the left ventricle.<sup>1</sup> Repeated cardiovascular examinations of this patient during the past four years have shown him to be in excellent physical condition and without cardiac symptoms. Other observers have reported similar experiences, Vaughan,<sup>2</sup> Constantini,<sup>3</sup> and Hesse<sup>4</sup> have collected many such cases from the literature.

The military surgeons have developed an extensive literature upon in-

juries to the heart by piercing instruments. If operated upon soon enough and before much hemorrhage has occurred, most such perforations of the heart do well and convalescence is prompt.

Rupture of the heart as the result of cardiovascular pathology is, however, almost always fatal. The explanation of the end-results of these two types of cardiac injuries lies perhaps in the fact that in the traumatic group the cardiovascular system is usually normal and unless the damage to the heart be excessive there is sufficient myocardial reserve power to maintain an adequate circulation. In the pathologic group, on the other hand, the rupture has occurred because of widespread myocardial involvement which has reduced the cardiac reserve to a dangerously low level, an adequate circulation under these conditions is thus impossible and death occurs.

The pathology underlying spontaneous rupture of the heart is apparently vascular in origin. Disturbance and interference with the coronary circulation quickly leads to under nourishment of the myocardium with an accompanying loss in functional ability. Such disturbances arise from sclerosis

\*From the Witkin Foundation for the Study and Prevention of Heart Disease, Beth David Hospital, New York City.

†Read in a Symposium on Heart Disease at the Metropolitan Medical Society, New York, Jan. 22, 1929.

and gradual stenosing of the coronary arterial tree. Where the process is equally distributed throughout the entire heart there may be no or very little manifestation of the condition and when found in the fifth and sixth decades may, with some justice, be considered as a normal phase of senescence.

Where, however, the sclerosing process appears unequally distributed in the coronary system, a sudden narrowing or complete occlusion of an artery may lead to prompt infarction of the area supplied by the affected vessel. The usual pathologic changes now take place as elsewhere in the body whenever an end-artery fails to carry blood to its part. In the heart, the ischemic area of infarction may become congested from venous back flow, there is extravasation of blood cells and a rapid destruction of collagen and later, of the myocardial fibers themselves.

If the infarcted area be of limited extent, the normal reparative process ends in fibrosis and scarring of the heart muscle, but when larger portions of the myocardium are involved, liquefaction necrosis occurs and a sterile abscess of the heart develops. The hazard of such an area of necrosis depends apparently not so much upon its size as upon its location. If it lies within the so-called "pressure zones" of the heart, danger of rupture may be very great. When it occurs in or near the conducting pathways of the heart, various disturbances of rhythm may occur and when it develops in the "silent areas" of the heart there may be no evidence of its presence.

The healing process may be active enough to absorb certain small areas of necrosis and the resulting scar when subjected to pressure may gradually stretch and lead to aneurysmal dilations of the heart wall.

Rupture of infarcted areas in the wall of one of the cardiac chambers is followed by immediate hemorrhage into the pericardium<sup>5, 6, 7</sup>. Instantaneous death usually occurs but the patient may go into profound shock and die a few hours later<sup>8, 9</sup>. Few cases have lived longer than twenty-four hours<sup>10, 11</sup>.

The cause of sudden death in these cases is apparently not well understood, hemorrhage into the pericardium itself is not sufficient to produce such extreme shock and death. As noted before, perforation of the heart by foreign bodies is not accompanied by this clinical picture. Moreover, the actual loss of blood in spontaneously ruptured hearts may be very small, in one case only 5 cc was found. In other cases from 50 to 200 cc were discovered.

The capacity of the normal pericardium is not great, experimentally in the cadaver, only 200 to 350 cc of fluid can be injected. Ordinarily the pericardium does not stretch quickly and while it is true that as much as 1,000 cc have been removed not infrequently in cases of hydropericardium, the capacity of the pericardium in this latter condition has been slowly and gradually extended<sup>12</sup>.

Hemorrhage into the pericardium cannot of itself be the explanation of the sudden death which occurs in spontaneously ruptured hearts. Other

factors, not the least of which is the associated pathology in the heart, must be considered. It has been previously indicated that when the myocardial reserve has not been lowered by undernourishment or disease, extensive damage may be sustained by the heart without loss of adequate circulation. Where, however, the myocardial reserve is low any sudden additional damage, be it ever so slight, may be sufficient to over-burden the circulation and cause shock and death.

Erdheim has repeatedly demonstrated spontaneous ruptures of either ventricle which barely admit the tip of a probe. On the other hand, large infarcted areas have been discovered in the walls of the ventricles in patients dying from extracardiovascular diseases.

These apparently paradoxical post mortem findings may be explained by assuming that the perforation regardless of its size is accompanied by unusual electrodynamic phenomena which cause a damaged myocardium to develop an ectopic rhythm and which may precipitate an attack of ventricular fibrillation with immediate death.

Mention has been made that where the sclerosing process has been unequally distributed throughout the coronary tree, the danger from infarction and its sequelae is greater than in the heart where the arterial degenerative process is more widespread. This fact corresponds very closely to the clinical observation that coronary artery sclerosis is more dangerous when it occurs in the fourth and fifth decades than in the sixth and seventh

The senescent heart is apparently better adapted to the new pathology than is the younger, more irregularly damaged cardiovascular system.

In addition to this type of the sclerosing process, syphilis of the cardiovascular system may produce a somewhat similar type of pathology. More often the luetic infection affects only the orifices of the coronary arteries and the patient exhibits the stenocardial syndrome, sudden death in such cases is usually due to occlusion of an entire coronary vessel in contrast to the other types of vascular degenerative change which pick out smaller subdivisions of the coronary tree.

The clinical picture of spontaneous rupture of the heart is not characteristic, the symptomology may be and frequently is referred to the gastro-intestinal tract. The patient complains of severe abdominal pain which is not readily localizable. He is nauseated and vomits, he rapidly goes into shock with cold cyanosed extremities and a livid pallor is noted. The pulse is rapid and often impalpable. The clinical picture may suggest in every way a ruptured gastric or duodenal ulcer. Symptoms may be referable to the chest, the patient complaining of terrific pain in the lower back or the axillae. The pain may be referred upward into the neck. Strangely enough, the precordial region may be entirely free from any pain or symptom. Extreme and rapid prostration is, however, a most constant finding. Death may occur promptly, in those cases where a diagnosis of ruptured ulcer has been made the patient may die upon the operating table, the sur-

geon being unfairly credited for the death

Auscultation of the heart is usually quite unsatisfactory, because of the patient's noisy respiration no heart sounds are audible. On close attention the basal heart sounds can be identified but rarely can the apical sounds be heard. Of unusual interest is the occurrence of a peculiar harsh and shrill murmur which is systolic in time; this murmur appears very close to the ear and its loudness is out of proportion to the character and intensity of the other heart sounds. I believe this murmur to be of great importance in the diagnosis of spontaneous rupture of the heart; it is not mentioned in the available literature but it has been noted six times in cases which subsequently have come to post mortem and in which pathologic perforations have been found. The peculiar quality of this murmur in conjunction with other cardiovascular findings is not readily forgotten once the clinician has discovered it.

While spontaneous rupture of the heart into the pericardium is not especially uncommon, rupture and perforation of the interventricular septum is apparently infrequent. Vaquez<sup>13</sup> mentions the possibility of septal rupture in acute tricuspid valvular infections, Cabot<sup>14</sup> describes an infarction and aneurysmal dilatation of the heart with involvement of the interventricular septum. Direct perforation of the septum alone has not been found in the literature. The following case is therefore of interest in that the diagnosis was suggested and made prior to death and the post mortem examination

II S, a man, age 52, was admitted to the Cardiac Service of the Beth David Hospital, October 29, 1928 (Hospital No 28-2658), at 11 30 A M., about one hour after I had seen him in consultation through the courtesy of the family physician, Dr Joseph Nisonoff. The patient's history was typical and is here related in some detail. He had previously enjoyed good health and was of rugged constitution. He had been awakened suddenly that morning with a severe cramp-like pain in the lower abdomen, he felt nauseated and vomited several times. The pain then became localized in the epigastric region and reached such an intensity that the patient rapidly became prostrated.

The family physician being unavailable, an emergency ambulance was called and the ambulance surgeon made a diagnosis of ruptured duodenal ulcer, he suggested immediate hospitalization and operation. The relatives objected on the ground that the patient had never had any previous gastro-intestinal symptoms. Two hours later the family physician arrived and he noted the patient's desperate condition and the very feeble heart action. He graciously suggested that I see the case and I reached the patient about four hours after the onset of the original attack of pain.

The patient was now in extreme shock, with cold clammy perspiration, deeply cyanosed and breathing with noisy respirations. There was no palpable pulse at the wrist; the superficial area of cardiac dullness appeared widened to percussion. No heart sounds were heard at the apex but the basal sounds were rapid (about 130) and of very poor quality. Unusual and striking was a very shrill systolic murmur which was heard equally well over the entire precordium. The peculiarities of this murmur have been described before. I made a diagnosis of spontaneous rupture of the heart and advised immediate hospitalization.

Directly upon admission to the hospital the patient was taken to the Heart Station where electrocardiographic studies were made. He was then quickly removed to his room and intravenous glucose and metaphyllin were ordered. At this time a member of the Interne Staff called attention to



the fact that the heart sounds were now more audible at the apex as well as at the base but the shrill superficial character of the murmur remained unchanged.

In commenting upon this I suggested that we might be concerned here with a rare phenomenon—an interventricular perforation. Assuming that the obscuring of the heart sounds could be due to two factors:

(1) The blood in the pericardium acting to dampen the sound waves in exactly the same manner as fluid does in pericarditis and (2) the loss of tone of the heart muscle as a result of the terrific injury it had undergone, with the return of the latter no change in the intensity of the heart sounds would be evident unless the quantity of blood in the pericardium be very small. The loud, shrill systolic murmur suggested a large perforation and if there was no or little blood in the pericardium, the rupture must be between two cardiac chambers, possibly in the interventricular septum.

The patient's condition at this time was so desperate that only emergency measures could be employed and he died about one-half an hour later. From the initial attack of pain to death was about five and a half hours.

The electrocardiographic studies (Fig 1) are of interest, characteristic T-wave alterations are noted especially well in Leads I and II. There was no axial deviation of the heart nor was there any delay in the QRS-complex. Simultaneous polygraphic tracings of the brachial artery taken with each of the three leads was normal. The rate was about 100 beats per minute and there was a normal sino-auricular rhythm.

This study points out clearly the value of electrocardiographic investigation in acute cardiac conditions. Experience has shown that there may be a considerable delay between the occurrence of cardiac damage and its manifestation by electrocardiographic

examination, several days or even weeks may be required before the characteristic changes found in the initial ventricular complex make their appearance.<sup>1</sup>

Discovery of T-wave alterations in this case suggest that the patient has had disturbances of his coronary circulation for some time but these changes have all taken place prior to the accident which led to death. On the other hand long standing areas of infarction when they occur in regions near the septum usually give unmistakable signs in the electrocardiogram: widening of the QRS-complex, splitting and feathering of the R-wave and bundle branch block are the usual changes that are found.

Post mortem examination was performed by the hospital Pathologist, Dr J Geiger. The pericardium was opened and found *free from blood*. The heart was slightly enlarged and weighed 310 grams. When it was opened a recent perforation large enough to admit one finger was discovered in the interventricular septum near the apex (Figure 2). Both coronary arteries were found to have irregular patches of sclerosis, the right was more involved than the left. In the terminal subdivision of the anterior descending branch of the right coronary artery was found a rather large thrombus which had apparently broken off from an adjacent area. The portion of the heart supplied by this vessel was pale and thinned out and appeared to be not very recent. In the apical part of the heart especially in the right ventricle was a large hemorrhagic area which was torn through

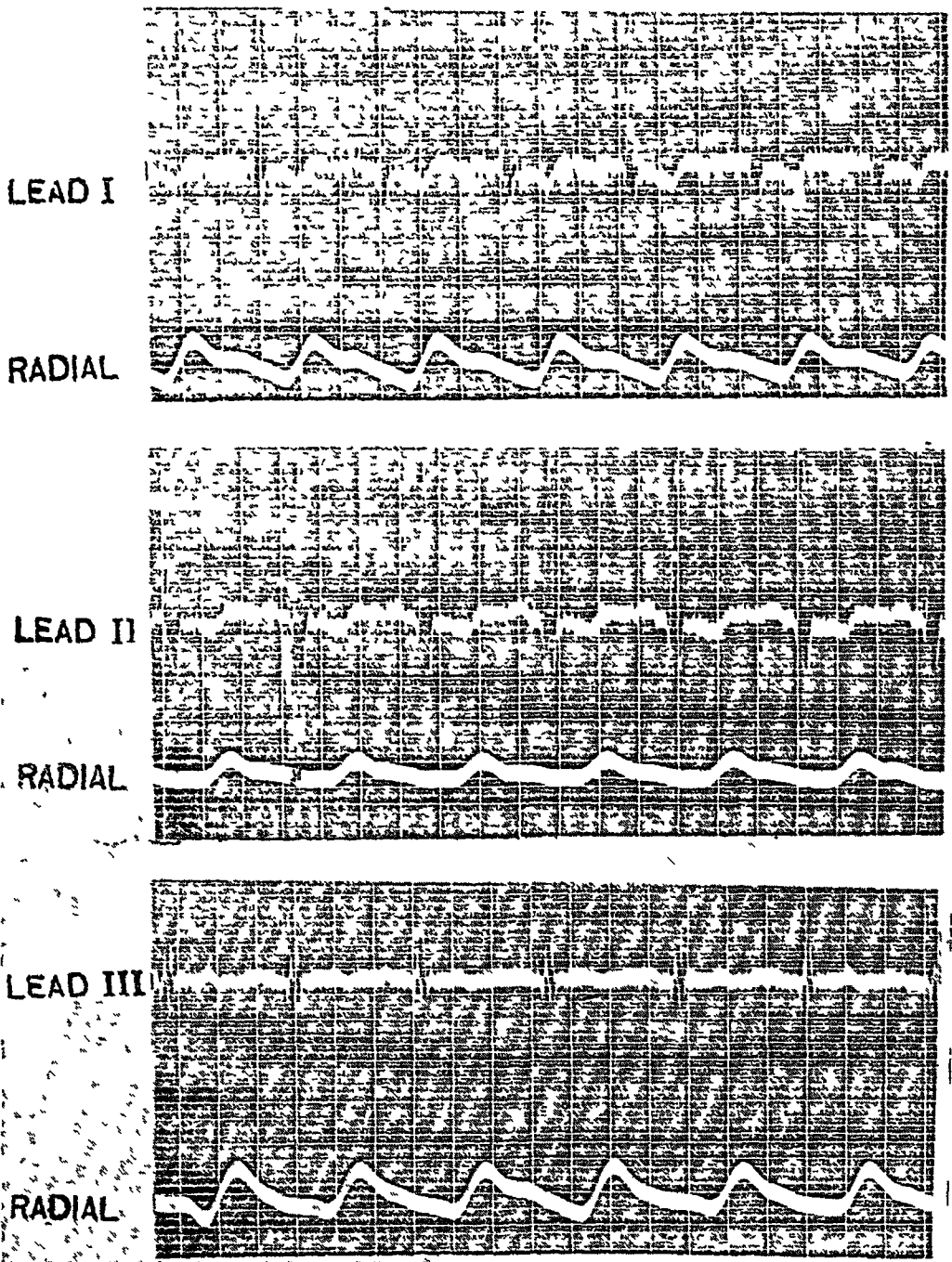


FIG 1 Electrocardiographic and polygraphic studies made about one-half hour before death, with the exception of the T-wave alteration the records do not suggest the widespread damage which is present in the heart. This is a common finding in recent injuries to the heart.



FIG 2 Photograph of heart seen from the left, the left ventricle is exposed. A flat wooden probe (x—x') is passed through the perforation at the bottom of the interventricular septum near the apex of the heart.

as it approached the septum. Several mural thrombi were found in the left ventricle. The valve mechanism was normal. The aorta was not enlarged but showed many atheromatous plaques.

#### SUMMARY

Spontaneous rupture of the heart is not an infrequent condition, it should

be suspected in all patients of middle age or older who present the clinical picture of sudden collapse and rapid prostration. The close resemblance to the symptomatology presented by ruptured gastric or duodenal ulcer can not be over emphasized, the extreme vasomotor collapse should put the surgeon on his guard. Discovery of a shrill

superficial murmur, systolic in time, which is out of proportion to the quality and character of the other heart sounds, should call to mind the possibility of spontaneous rupture of the heart

Hemopericardium always accompanies spontaneous rupture of the heart to a greater or lesser degree, but the amount of blood in the pericardium apparently bears no relation to the cardiovascular reaction to the injury

Prognosis is usually fatal in contradistinction to heart injuries as the result of trauma

In the case presented, the rupture was between two cardiac chambers instead of into the pericardium, while this condition must be extremely rare, the outlook and pathology is the same. To those interested in deductive diagnosis, rupture of the interventricular septum presents a fertile field for speculative investigation

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# A Clinical Study of a Graphic Method of Recording Blood Pressure\*

By LOUIS FAUGERIS BISHOP, M.D. and LOUIS FAUGERIS BISHOP, JR., M.D.,  
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HALL'S demonstration in 1733 proved that the movement of the blood carried with it a necessary consequence, that of pressure. This was made known one hundred years after the discovery of the circulation of the blood by Harvey, but another hundred years elapsed before this fact was given serious consideration. In 1828 Poiseuille introduced the mercury manometer of U form by which he was able to study blood pressure within a circumscribed space. Coagulation was retarded by sodium bicarbonate, a method in use today. All this work paved the way to newer discoveries and in 1847 Ludwig made use of the "kymographion," the forerunner of all modern graphic methods of precision. This earliest instrument obtained a pressure tracing from an open artery through a recording manometer, the tracing being made upon a revolving cylinder. It, however, recorded only a mean blood pressure and very elaborate compensatory adjustments were needed to obtain correct readings.

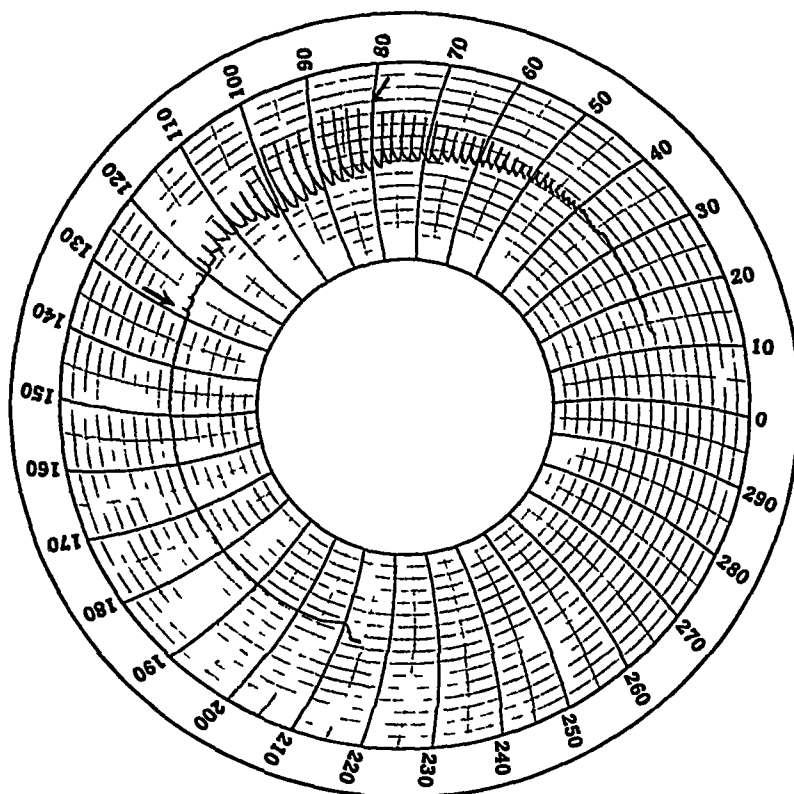
The work of Ludwig, in physiology, with his kymographion, made itself

felt as a stimulus in the field of clinical medicine. A large number of further steps led up to the development of clinically useful apparatus. Riva Rocci's invention of a cuff and bulb device was the outstanding achievement in this work.

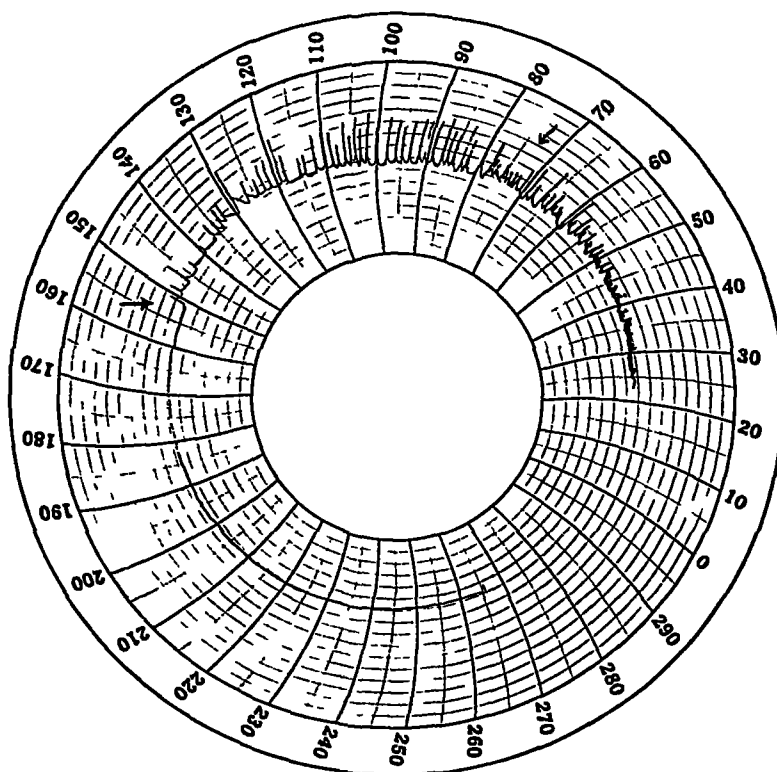
The further addition of devices for automatic record of blood pressure has greatly enhanced this work. Jacquet invented the sphygmotonograph in which he used the stylet of a metal manometer, which communicates with the brachial cuff and records directly on the tracing. Metal manometers, however, require standardization. An instrument, devised by Bingel, records every pressure change of 10 mm by the interruption of an electric current. Another sphygmomanometer, that of Gibson, consists of a mercury manometer, with a double U-shaped tube. In the reading the abscissa must be doubled. The height of the mercurial column is automatically recorded, thus avoiding the personal equation. The instrument is accurate, but somewhat bulky. C. Singer has devised a very similar mechanism. Erlanger's apparatus is more suitable for laboratory than clinical use, on account of its complexity. Time and skill are needed to manipulate it, but the records are

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\*Presented before the Boston meeting of the American College of Physicians, April 9, 1929.



GRAPH I—Normal blood pressure curve taken with recording machine  
Systolic 130—Diastolic 80



GRAPH II—Blood pressure curve from case of auricular fibrillation Complete  
irregularity in width and height of waves Systolic 130—Diastolic 75

very accurate. Polygraphic attachments can be included and used for pulse tracings. The systolic readings come 5 mm higher than the Riva Rocci, and the diastolic vary from 5 to 15 mm. The Uskoff sphygmotonomograph, also, was devised for both blood pressure and pulse readings. It simultaneously records: (a) blood pressure in mm Hg, (b) carotid pulse, (c) pulsation from brachial artery, (d) time in 1/5 second.

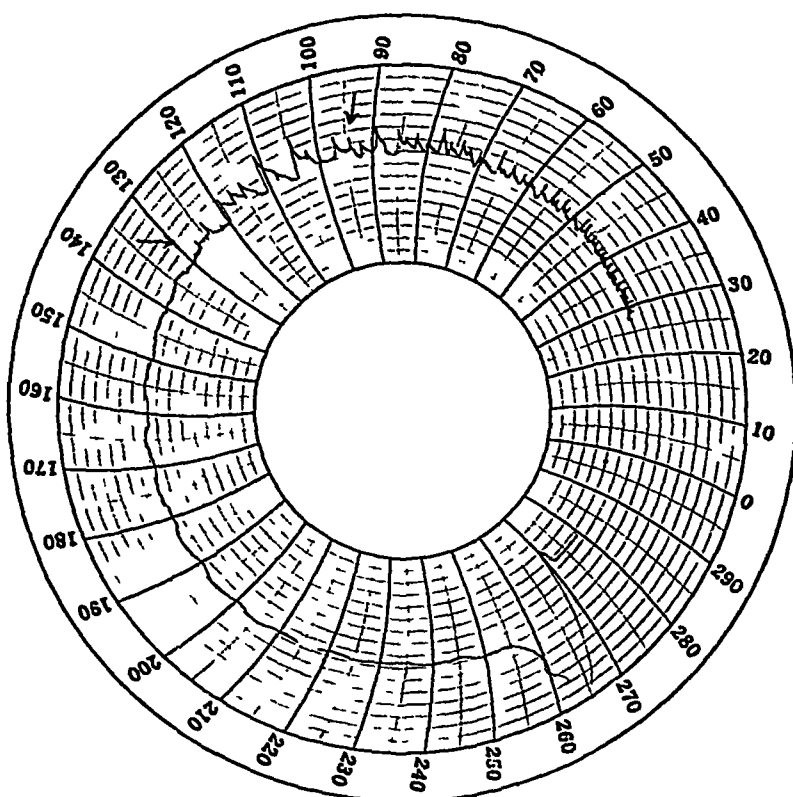
The graphic instrument of Silbermann is equipped with a radial and a brachial cuff, a mercury manometer, a float, a receiving drum for smoked paper and a registering device. The method of Brugsch consists of a U-shaped manometer and a revolving drum covered with white paper, ruled in cm spaces. Muenzer has an elaborated and complicated instrument which he calls a sphygmotomograph. The pulsations pass from the cuff through a balloon to the recording kymograph, the latter has two speeds, a slow one for blood pressure and a rapid one for pulse tracings.

Fleischer's instrument is somewhat similar, but he uses a metal cylinder, containing a celluloid cylinder, the latter floats in a layer of oil. The air from the cuff imparts the pulsations to a counterweighted lever, thence by a wire to the recording needle. In an ingenious little instrument by Bussemius, another principle is used, that is, he eliminates driving force and simply lets a narrow upright supported strip of paper fall by gravity at a graduated rate past the pulsating tambour. The strip falls at 1 mm per second. This device records both systolic and diastolic pressure. Another instrument,

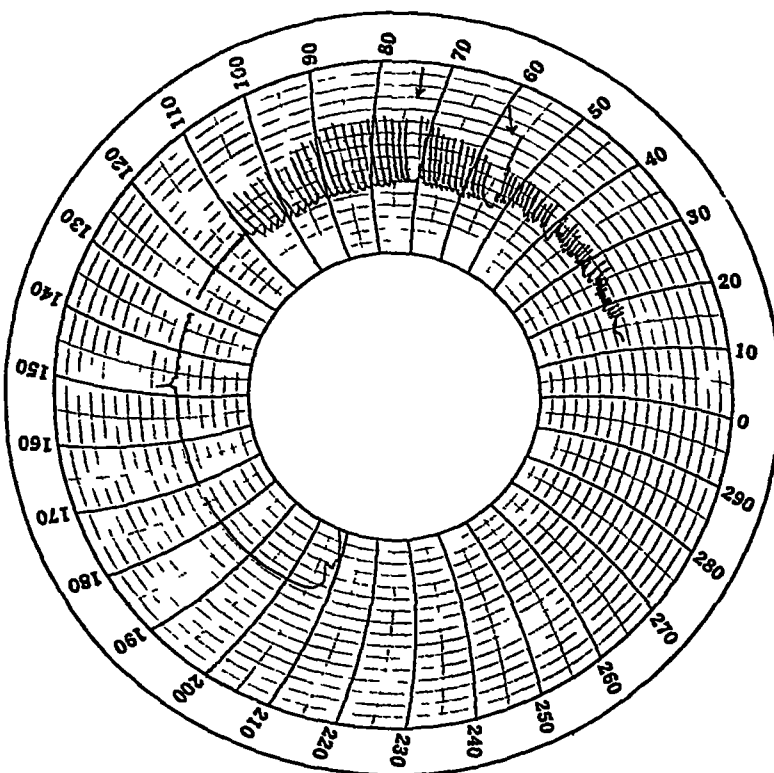
that of Wysbauw, is a modification of Erlanger, but has a double cuff which gives more accurate systolic readings.

Recently, Dr. L. A. Amblard of Paris, a pupil of Potam, has invented the "sphygmometoscope," a device for recording both systolic and diastolic pressure, also a pulse tracing. This device consists of an arm piece, a compression apparatus and a very sensitive manometer. A rigid leather band holds two cuffs, which can be inflated without touching. The inflating bulb has a stop cock, with a turning device on an index, a, b, or c. (a) is the inflation position, (b) the deflation, at (c) only the lower cuff communicates with the manometer. The machine has two speeds, viz. one and three centimeters per second. A stylet can be moved over the face of the tambour at any part. The first abrupt increase in the tracing indicates maximal pressure, the first abrupt decrease equals minimal pressure.

In our study of graphic methods we have used the Tycos Recording Sphygmomanometer, one of the most recent on the market. The tracings are made directly on the revolving disk, and are purely pressure graphs caused directly by the arterial pulsations, and do not represent units of time or of time and pressure. No clock or motor is used, but instead, a small stream of air escaping from a light collapsible metal tube sets the kymograph in motion. Decrease of pressure of the cuff round the brachial artery causes deflation through the light tube. Diminishing pressure in the arm band allows the arterial force to be felt, and to be imparted to the



GRAPH III—Blood pressure curve from case of auricular fibrillation. Complete irregularity in width and height of waves. Electrocardiogram revealed an associated heart block. Systolic 125—Diastolic 95



GRAPH IV—Blood pressure curve illustrating premature contraction occurring during the recording. Systolic 110—Diastolic 65



pen of the oscillometer, which in turn records the tracing on the moving disc.

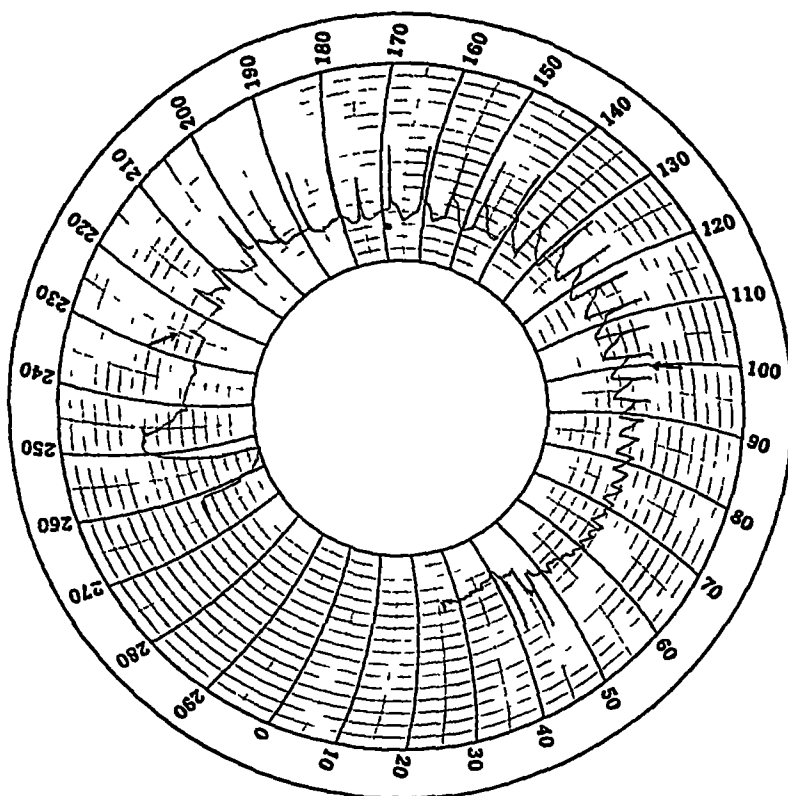
A sleeve for the patient contains an upper and a lower cuff. The sleeve is fitted snugly to the arm just above the elbow and when inflated should just suppress the pulsation of the brachial artery. The sleeve adjusted, the patient is told to keep quiet and relaxed, and sufficient inflation having been secured, deflation is commenced by opening a valve. The puff of escaping air at once starts the disk revolving. The first impact to occur against the upper, or filter cuff, is the thud of the closed artery, which causes a slight pulsation—the so-called “hydraulic ram wave,” which registers itself on the pointer and traces on the graph a series of short spikes directed inward toward the hub of the disc. As soon, however, as the surplus pressure of the cuff has been used up, that of the artery is released and begins to make itself felt. By this time the pressure of the upper cuff is lessening and allows the waves to pound upon the lower cuff. The effect of this is to set up a direct record, observable on the chart as a series of spikes pointed toward the periphery of the disc. What this really means is that systolic pressure is tracing its direct autograph on the diaphragm. Without manipulation this would naturally appear as a series of waves, but a method of so timing the rotation of the chart in relation to the oscillations of the pen has been worked out, so that, instead of waves, a series of spikes is produced and the *height of the spike*, which is an important feature, is brought into prominence.

The first spike pointing toward the

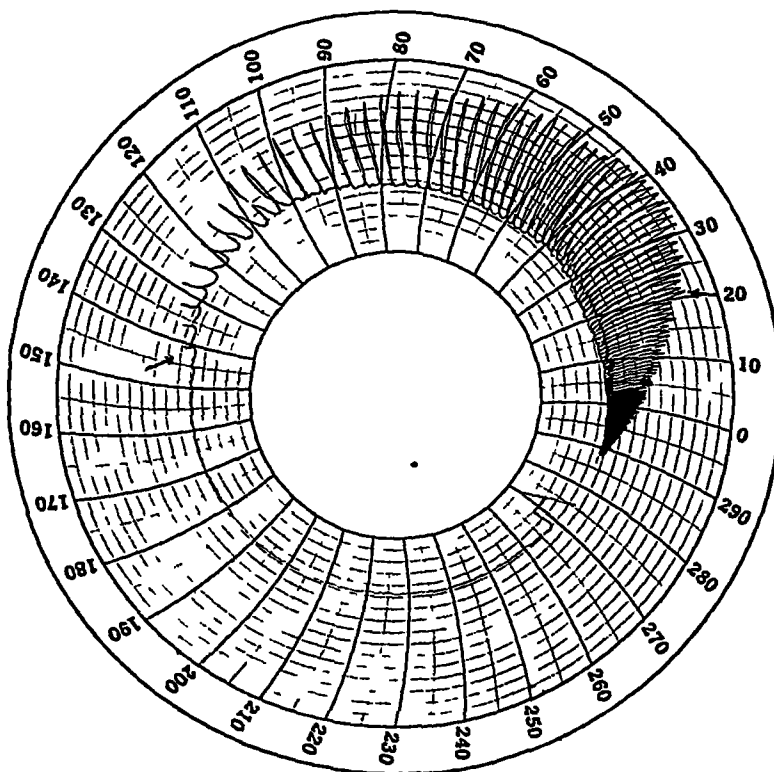
periphery traced bears relation to the first systolic sound. After the first spike the general character of the curve in this instrument is similar to that shown in other pressure instruments. The increase of pulsation in the released vessel under the cuff causes higher and higher spikes up to a certain point, at which they are seen to decrease in height and the peaks to become wider at the base. The first definitely shortened spikes and leveling corresponds to the phase of diastolic pressure and corresponds to the transaction of the third and fourth phase. We regard the first typical lowered and levelled spike as indicating diastole.

As has been said, the tracing is expressed in terms of pressure only. The chart is of disc shape and moves with angular motion, thus giving direct rates of speed to points of varying distance from the center. Second, the speed and the retardation are not uniform and these factors may be so adjusted as to bring out features in the tracing which it is desirable to emphasize and to lessen masking effects such as those produced by respiration.

The design of the cuff has been carefully worked out. According to von Recklinghausen, the narrower the cuff, the greater the pressure, and vice versa. The cuffs are standardized in such a way that the width affects pressure to the extent that the first spike on the tracing corresponds to the first sound, as heard in the normal individual by the normal ear. The listener's ear was standardized by the audiometer, and a subject was used in whom the sounds approached classic regularity.



GRAPH V—Blood pressure curve illustrating hypertension on recording machine  
Systolic 225—Diastolic 100



GRAPH VI—Blood pressure curve from patient with aortic insufficiency  
Systolic 190—Diastolic 20

During the past year we have used this graphic method in our office for the recording of about five hundred records in conjunction with our practice. We have carefully checked the reading thus made with the Becton-Dickinson manometer, and they have agreed very closely with our charts.

The few conclusions we would like to make are

1 Removal of the personal equation in blood pressure is probably the most important point in the use of a graphic method

2 Some conclusions can be drawn in regard to the cardiac arrhythmias from the records of blood pressure

made with this instrument, but in no sense does it replace the electrocardiograph for this purpose

3. The curves shown are purely graphs of blood pressure recording the pulsations of the brachial artery. They do not show any intracardiac manifestations

4 In cases where ordinary methods are very difficult, as, for example, auricular fibrillation and paroxysmal tachycardia, the graphic method is of great value

5 Should the future bring forth an instrument which was less complicated and did not require such skillful manipulation a great advance would be made in its clinical use

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# Endogenous Obesity—A Misconception\*

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THE physician who prescribes a low calorie diet to reduce the weight of his obese patients frequently deals with subjects who fail to lose weight during the period of observation. And the writers have satisfied their desire for an explanation of this seemingly paradoxical phenomenon by attributing it to abnormality of the endocrine glands—in particular the hypophysis, the thyroid, and the gonads. The logical conclusion to be reached from such a position is that these patients are the unfortunate victims of constitutional disease that unrelentingly causes a progressive deposition of adipose tissue, independent of activity or dietary habit. It is not to be expected that restriction in food will reduce the weight of such individuals. Those who support this hypothesis have placed themselves in a precarious position, since they are in fact denying the principle of the conservation of energy, and are disregarding the quantitative facts that form the foundation of our knowledge of energy transformations by man.

The sceptic who has not witnessed this apparent contraversion of natural

law might be unwilling to admit its occurrence. But that is not the explanation. There can be no doubt about the fact that individuals sometimes maintain their weight while subsisting on very low calorie diets. Fig. No. 1 is a standard example of this phenomenon from our practice. After it had been demonstrated that 2300 calories maintained the weight of this obese young woman, the diet was abruptly reduced to 1500 calories. You note that this change caused an abrupt decline in weight lasting only two days. During the next eleven days the patient failed to lose weight in spite of the unquestionable caloric inadequacy of the diet. Furthermore, undernutrition diets may even be accompanied by gain in body weight as Fig. No. 2 demonstrates. This patient gained three pounds in nineteen days even though the diet was far below the requirement for maintenance.

The searcher after truth may question whether the patients, from whom such paradoxical weight records have been obtained, have not secured an extra supply of food without the knowledge of the attendants or whether the diet given the patient contained more energy (through an error) than was ordered. We have avoided these two sources of error by studying our

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\*Presented to the American College of Physicians, Boston, April 12, 1929.

†Department of Internal Medicine, Medical School, University of Michigan.

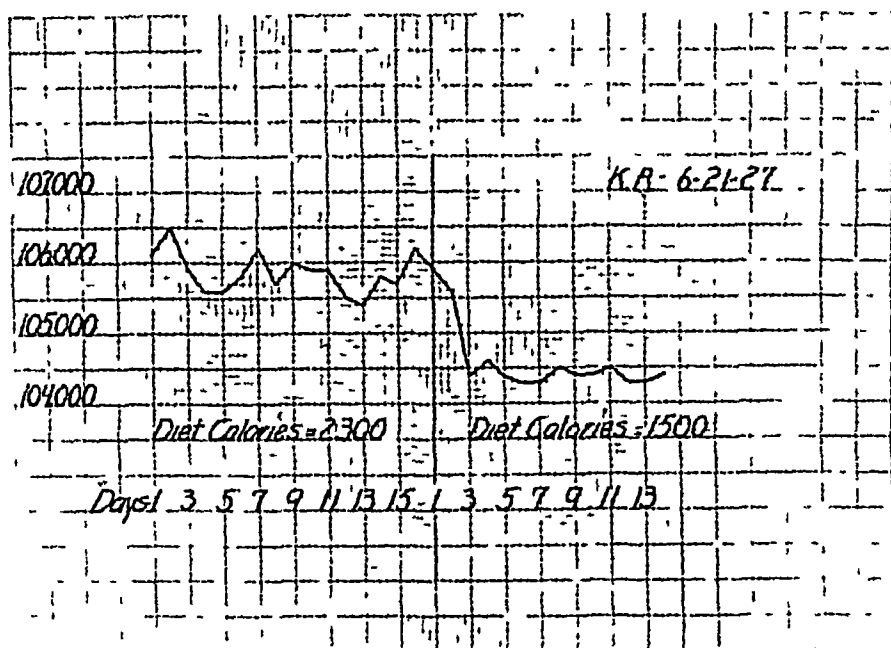


FIG 1 An obese young woman maintains her weight, first on 2,300 calories and then on 1,500 calories

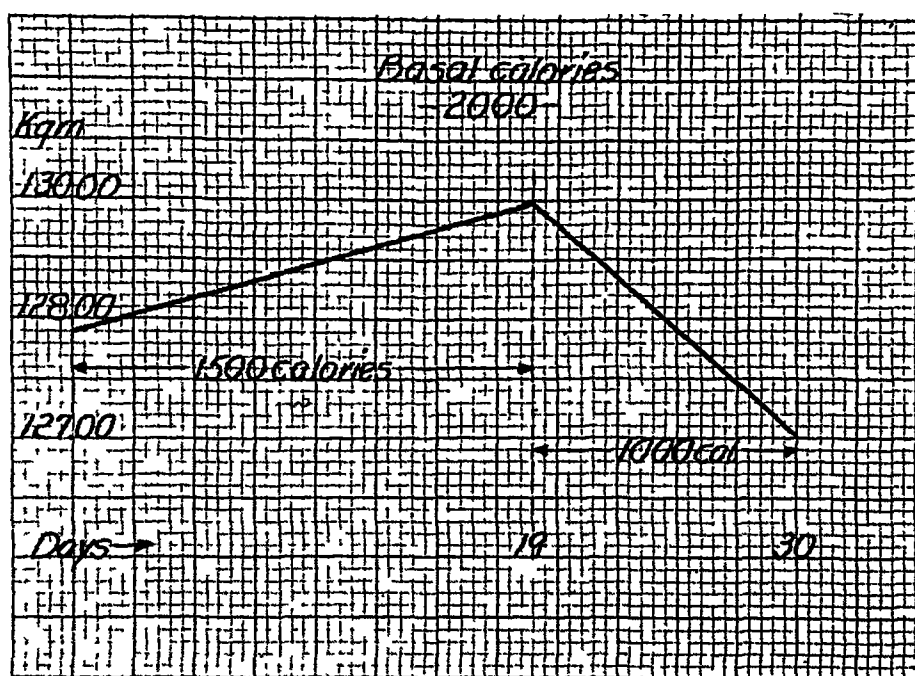


FIG 2 An obese subject gains weight on a diet far below the requirement

patients individually in a specially designed room which made it possible to observe the subject continuously throughout the twenty-four hours. And we have checked the diets by analyzing samples in our own laboratory. It is certain that the patients received only the energy allowances prescribed by us.

In order to predict the change in weight of an individual who receives food of known caloric value, it is necessary to measure the outflow of energy throughout the period of observation. In the past this requirement has been met only in part. It has been customary to determine the basal metabolic rate and then to make a sophisticated guess regarding the extra calories required for activity and the metabolism of the food. Fortunately we were able to avoid the inaccuracy of such a compilation by modifying a method for measuring heat loss recently described by Benedict and Root<sup>1</sup>. They have shown that the weight of the Insensible Perspiration is parallel to the metabolic rate in the basal state, when certain easily obtained conditions are set up. If the gain or loss of weight for each twenty-four hours is corrected for the weight of the food and drink on the one hand, and for the weight of the urine and feces on the other hand, the resultant is the weight of the Insensible Perspiration for the period.<sup>2</sup> By reference to the appropriate table this value may be directly converted into a statement of the total loss of heat for the twenty-four hours.

With this method at hand we undertook a study of the changes in weight in a normal young man. He remained

quietly in bed during the investigation in order to make the requirement for energy as uniform as possible. His diet was restricted to milk and sugar and was always weighed on a good balance by one of us. In addition, the milk was analyzed for nitrogen, fat, solids, and carbohydrate daily.

Under these carefully controlled conditions, it was possible to show that the normal subject would also maintain his body weight or even add to it while he was being underfed. Fig. No. 3 records a gain of 475 grams in five days even though the daily outflow of energy from the subject amounted to 1688 calories whereas he received only 1078 calories. In the face of a daily caloric deficit of 600, he actually added one pound to his weight in five days.

This response of the normal man makes it clear that the ability to maintain the original weight when the diet yields less energy than is used, is not characteristic of any particular type of obesity. Further study showed that it is dependent upon the composition of the diet. Fig. No. 4 represents three consecutive periods in the record of an obese young woman. During the first week she maintains her weight on a diet of 2500 calories. For the next ten days, a diet high in carbohydrate (260 grams daily) that yielded about 1800 calories, was accompanied by a slow steady fall in weight. A sudden shift to a diet of about the same caloric value, but very low in carbohydrate (42 grams daily) resulted first in a rapid loss of weight of short duration, followed by a period nine days long during which no weight was lost. Thus an individual whose

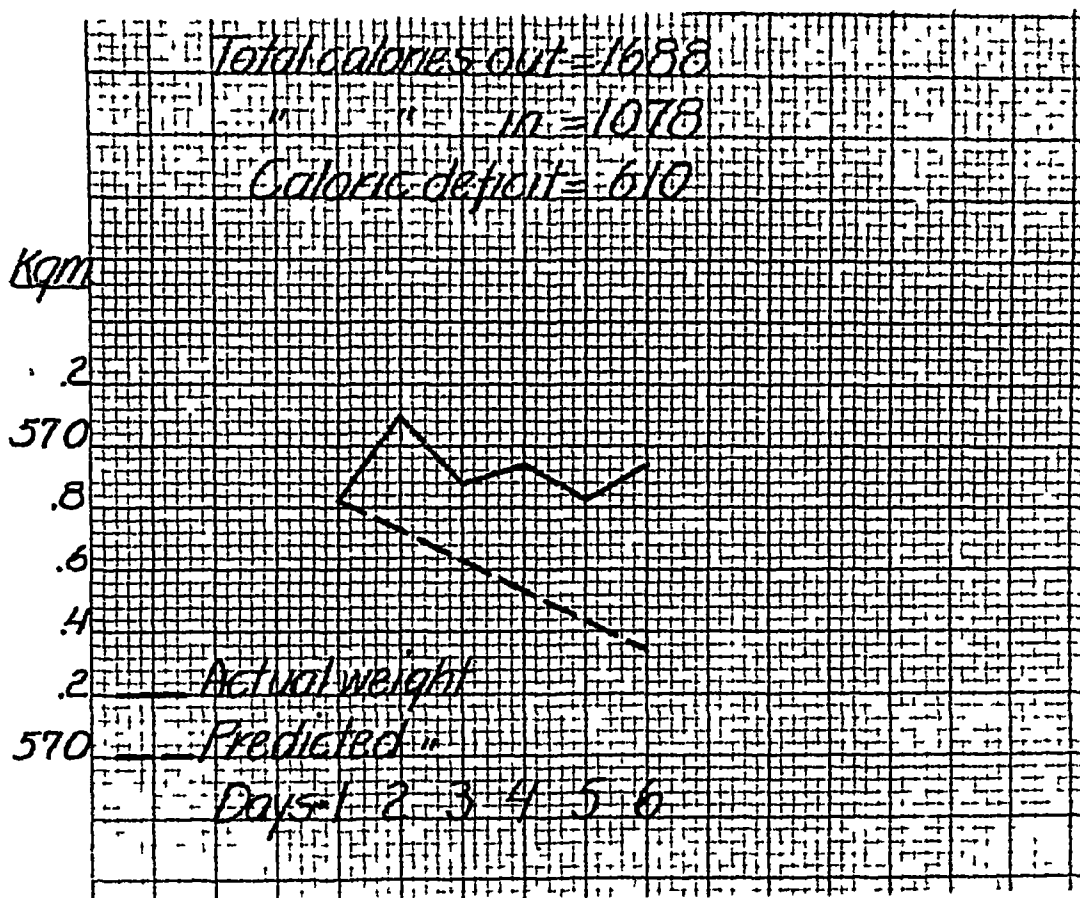


FIG 3 A normal man gains one pound in five days, on a diet that caused the destruction of one pound of body tissue

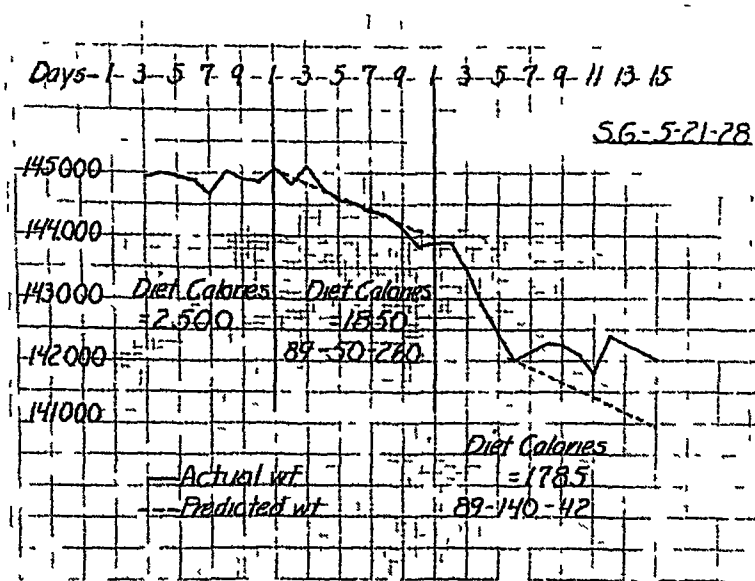


FIG 4 The composition of the diet determines the shape of the weight curve

maintenance requirement was 2500 calories was first made to lose weight progressively and then to maintain her weight, by the successive use of two diets of about equal energy value but widely separated by their content of carbohydrate

Day to day changes in weight do not reflect the disproportion between inflow and outflow of energy

How long may an individual maintain his weight in the face of a diet deficient in calories? Does this process continue indefinitely? The literature gives no answer to these questions. Our own observations have shown us that the failure to lose weight is only a matter of days. Thus far the longest period observed by us has been sixteen days. Usually it is shorter. A

good example of this phenomenon is seen in Fig No 5. This very obese young woman lost essentially no weight for ten days on a diet containing only a little more than half the caloric requirement, in fact she actually made a significant gain in the first two days. Then an abrupt change occurred, consisting of a continuous rapid loss of weight, until, on the thirteenth day, she weighed approximately what had been predicted for her. The prediction was made by converting the caloric deficit for thirteen days into the weight of the adipose tissue that would be oxidized by the subject if her metabolism conducted itself in accord with the physical principles that apply in normal persons.

These departures from the simple

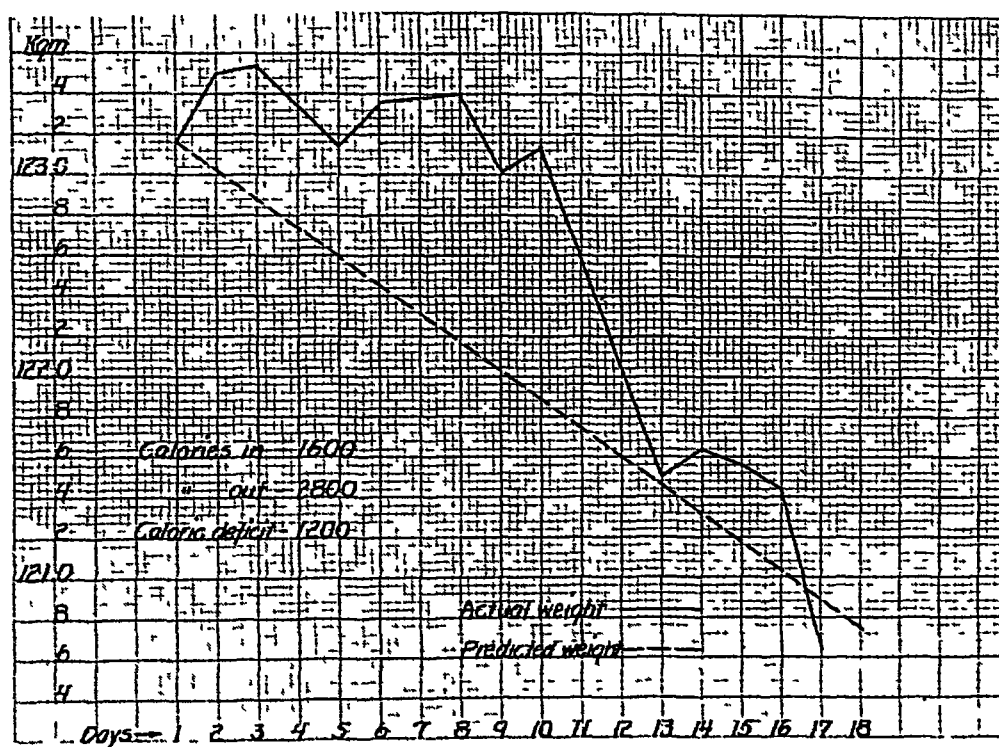


FIG 5 An obese subject first maintains her weight and then loses weight so rapidly that the total loss corresponds with the prediction



straight line decline in weight are then firstly of short duration, and secondly always compensated for by a subsequent excessive loss of weight until the total loss corresponds with the expectation. This phenomenon may be produced in the normal subject by suitable adjustment of the diet, accordingly it has no specific significance when it occurs in the obese.

In order to do away with any mystery in connection with the maintenance of weight when the subject is being undernourished, it is in the first place necessary to be able to calculate precisely the weight of the body tissue oxidized to furnish that portion of the energy given out but not contained in the diet. Briefly, this may be done by comparing the total heat production and the total nitrogen output with the energy value and the composition of the diet. This gives the composition and the amount of body tissue destroyed. That is, the predicted loss of weight assuming that no interfering events occur. But the actual changes in weight do not, as a rule, correspond with this simple prediction, whether the subject be obese or normal, undernourished or overnourished.

Since very slight differences in the water content of a mass of protoplasm the size of a human being will amount to pounds in terms of weight, we undertook the difficult task of determining the water exchange<sup>3</sup> in our subjects. With this data at hand it became evident that the organism is very unstable in regard to water, that even when the body is in nutritional balance, it may increase or diminish its percent of water from day to day.

When undernutrition is effected by

means of a diet low enough in carbohydrate to cause a large destruction of glycogen, the subject loses weight rapidly for several days while the body is giving up its glycogen, then abruptly enters a second phase during which there is a progressive retention of water by the tissues. After a number of days, this extra water is all given off and at the end of this third phase, the total loss of weight from the inception of the underfeeding corresponds with the calculated weight of the tissue destroyed. The actual results of this type of investigation are exemplified in Table No. 1 and Fig. No. 6 for the normal subject, and in Table No. 2 and Fig. No. 7 for an obese girl with hypophyseal disease.

During the period from which Table No. 1 and Fig. No. 6 was constructed, the normal man dissipated 1818 calories daily. He received 1079 calories in his diet, therefore he obtained 739 calories from the oxidation of his own body tissues. Since he put out 118 grams of nitrogen daily but ingested only 101 grams, he must have lost from his body the protein which contained the 17 grams of nitrogen not furnished by the diet. This protein weighed 11 grams ( $17 \times 6.25$ ), but as it existed in the living moist state in the body, it weighed 44 grams. The combustion of this 11 grams of protein yielded 44 of the 739 calories derived from the destruction of body tissue. The remaining 695 calories came from the oxidation of 77 grams of fat, which in the form of adipose tissue weighed 85 grams. The weight of the body tissue destroyed each day was accordingly 129 grams.

If 129 be subtracted from the 1818

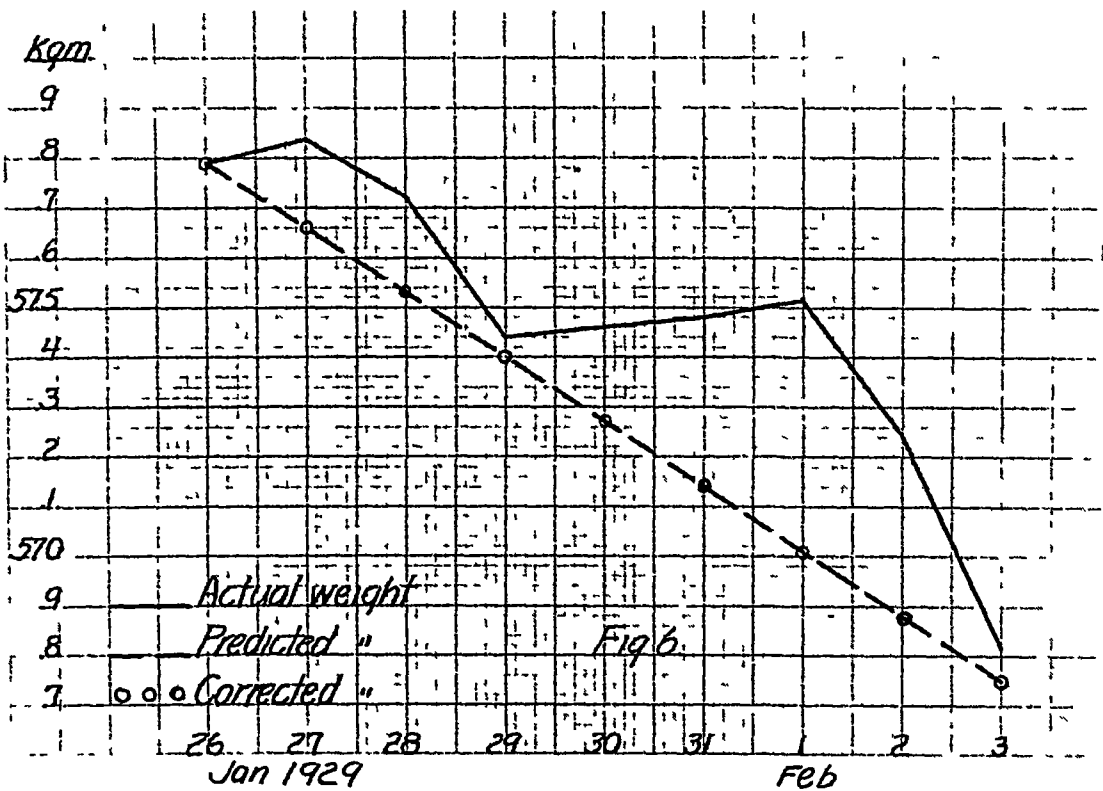


FIG 6 A normal man gains weight while being undernourished, due to continued retention of water

recorded on actual weight of the subject at the beginning of the period, one obtains a value that indicates what he would have weighed the second day—if that weight reflected merely the loss of body tissue. For example, the weight on the first morning was 57.790 kilograms. The destruction of 129 grams of body tissue in twenty-four hours, would reduce the weight on the second morning to 57.661 kilograms (the Predicted Weight). But the man actually weighed 57.840 kilograms at that time. He had gained 50 grams instead of losing 129 grams. If now the water exchange for this twenty-four hours be examined, it is seen that he added 175 grams of water to his body. The subtraction of this gain in water from the actual weight on the

second morning, gives 57.665 kilograms (Corrected Weight), which is what he would have weighed if no water had been retained. This corrected weight is essentially the same as the predicted weight. The evidence accordingly shows that the difference between the actual and the predicted weight was entirely due to retention of water, and supports the statement that the organism did lose tissue in amounts that coincide precisely with the values predicted from the conditions of the experiment.

The application of this same type of study to the obese girl with disease of the hypophysis accounts with equal success for the fact that she lost no weight for sixteen days even though she was destroying 181 grams of body

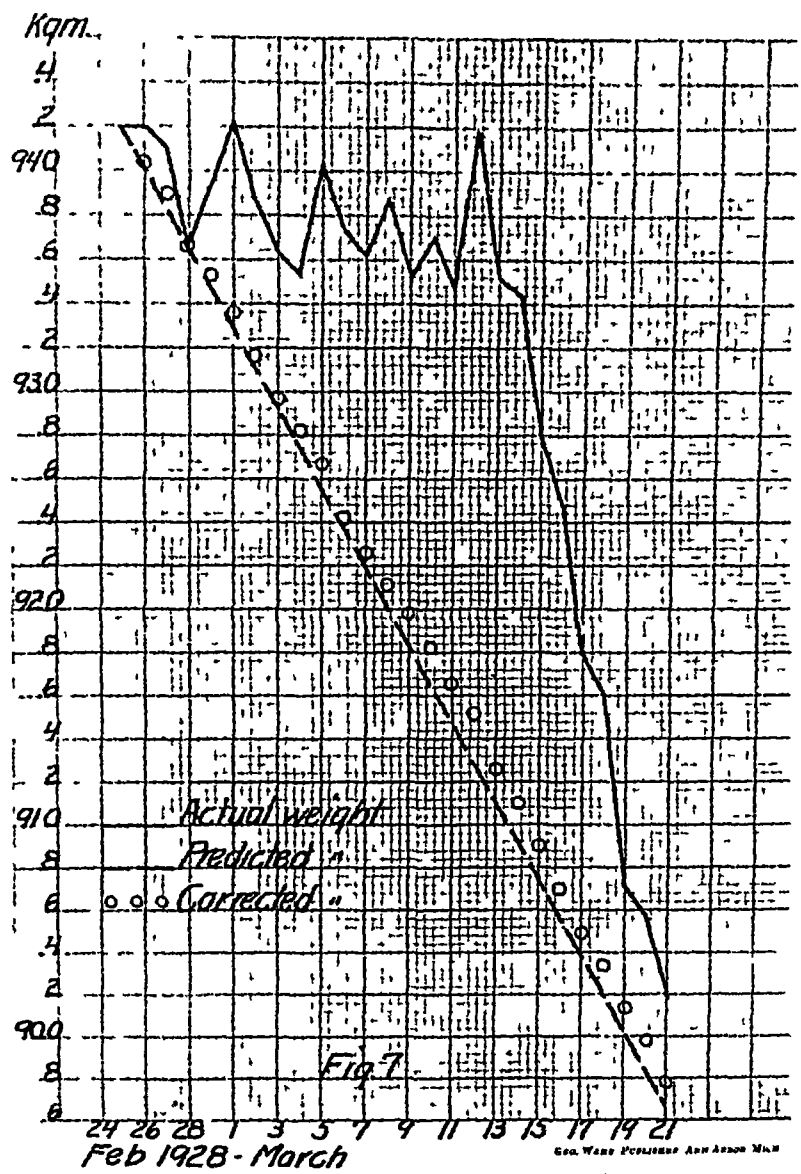


FIG 7 The same phenomenon in the case of an obese subject with endocrine disease

tissue daily, and would have lost 2896 grams if the percentile saturation of her body had remained constant. But in fact she retained water in such large amounts that her day to day weights gave no indication that body tissue was being oxidized as predicted.

SUMMARY

It is hoped that this brief review of our studies has made it clear that, when undernutrition is in effect

(1) An accurate knowledge of the composition of the diet on the one hand, and a satisfactory statement of the total loss of heat and total nitrogen output on the other hand, make it possible to obtain precise information about the kind and amount of body tissue that the subject must destroy to furnish the caloric deficit.

(2) An accurate tabulation of the water exchange shows that body

TABLE I  
COMPARISON BETWEEN PREDICTED WEIGHT AND CORRECTED WEIGHT IN THE NORMAL SUBJECT

Date	Actual Weight Kilos	Change in Actual Grams	Weight Predicted Grams	Water Retention or Loss Grams	Corrected* Weight Kilos	Predicted** Weight Kilos
1-26-29	57 790					
1-27-29	57 840	+ 50	—129	+175	57 665	57 661
1-28-29	57 725	—115	—129	+ 33	57 517	57 532
1-29-29	57 440	—285	—129	—147	57 379	57 403
1-30-29	57 465	+ 25	—129	+139	57 265	57 274
1-31-29	57 480	+ 15	—129	+129	57 151	57 145
2- 1-29	57 515	+ 35	—129	+175	57 011	57 016
2- 2-29	57 245	—270	—129	—153	56 894	56 887
2- 3-29	56 815	—430	—129	—293	56 757	56 758

\*These are the actual weights, plus or minus water lost or retained by the organism during the preceding twenty-four hours

\*\*This is what the subject would have weighed on each day, if his weight had been affected solely by the loss of body tissue destroyed during the preceding twenty-four hours

TABLE II  
COMPARISON BETWEEN PREDICTED WEIGHT AND CORRECTED WEIGHT IN AN OBES SUBJECT

Date	Actual Weight Kilos	Change in Weight Actual Grams	Predicted Grams	Water Retention or Loss Grams	Corrected* Weight Kilos	Predicted** Weight Kilos
2-25-28	94 200	0	-181	+157	94 043	94 019
2-26-28	94 200	— 85	-181	+ 66	93 892	93 838
2-27-28	94 115	-480	-181	-249	93 661	93 657
2-28-28	93 635	+300	-181	+448	93 513	93 476
2-29-28	93 935	+280	-181	+428	93 365	93 295
3- 1-28	94 215	-350	-181	-144	93 159	93 114
3- 2-28	93 865	-230	-181	— 39	92 968	92 933
3- 3-28	93 635	-110	-181	+ 42	92 816	92 752
3- 4-28	93 525	+500	-181	+650	92 666	92 571
3- 5-28	94 025	-290	-181	— 48	92 424	92 390
3- 6-28	93 735	-110	-181	+ 44	92 270	92 209
3- 7-28	93 625	+260	-181	+396	92 134	92 028
3- 8-28	93 885	-360	-181	-210	91 984	91 847
3- 9-28	93 525	+170	-181	+338	91 816	91 666
3-10-28	93 695	-225	-181	— 79	91 670	91 485
3-11-28	93 470	+720	-181	+872	91 518	91 304
3-12-28	94 190	-665	-181	-411	91 264	91 123
3-13-28	93 525	— 90	-181	+ 71	91 103	90 942
3-14-28	93 435	-640	-181	-434	90 897	90 761
3-15-28	92 795	-300	-181	-107	90 704	90 580
3-16-28	92 495	-700	-181	-486	90 490	90 399
3-17-28	91 795	-195	-181	— 48	90 343	90 218
3-18-28	91 600	-875	-181	-673	90 141	90 037
3-19-28	90 725	-150	-181	+ 13	89 978	89 856
3-20-28	90 575	-380	-181	-191	89 789	89 675
3-21-28	90 195					

\*These are the actual weights, plus or minus water lost or retained by the organism during the preceding twenty-four hours

\*\*This is what the subject would have weighed on each day, if his weight had been affected solely by the loss of body tissue destroyed during the preceding twenty-four hours

weight is the resultant of two factors, namely (1) gain or loss of tissue and (2) a gain or loss of water. The loss of one and a gain in the other may neutralize each other, or a large retention of water may cause a gain in weight even though body tissue has been consumed, and may lead an observer, who fails to take water exchange into account, to draw erroneous conclusions.

(3) The response of various types of obese people does not differ from that of normal people. All of them oxidize body tissues in accord with the prediction from the caloric deficit.

#### CONCLUSIONS

Obesity is always caused by an overabundant inflow of energy. The excess is deposited as adipose tissue. This disposition arises from a variety of conditions that may be thought of under two general headings. The first group includes the various human weaknesses such as over-indulgence and ignorance. The second group is composed of conditions that cause a decrease in the requirement for energy, such as lessened activity or lowering of the basal metabolic rate for any reason. If the long established food habits do not respond to this lessened demand, obesity is inevitable.

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# The Use of Sodium Malate Combinations as a Dietary Substitute for Sodium Chloride.

By JOHN C. KRANTZ, JR., Ph D., *Baltimore, Md*

**I**NTRODUCTION The prevalence of the prescribing of the diet of salt restriction for patients suffering with chronic interstitial nephritis, edema or hypertension is emphasized by Allen<sup>1</sup> who estimates this number to be more than two million in the United States. Although the most enthusiastic advocates of the diet of salt restriction claim beneficial results in cases of nephritis, edema and hypertension, little evidence is available in the literature indicating work upon the production of sodium chloride substitutes to increase the palatability of the salt restricted diet. In 1912 Javal<sup>2</sup> suggested the use of sodium bromide or iodide to improve the taste of unsalted bread. In many respects these compounds are as objectionable in the foregoing conditions as sodium chloride itself. Tueteur<sup>2a</sup> described a double calcium salt of polyaminic acid which he claims to have a salty taste.

With the purpose of discovering some compound (or mixture of compounds) that would play the rôle in the diet of salt restriction, that saccharin plays in the diet of sugar restriction, this investigation was begun.

*Selection of Compounds* The outstanding characteristic of a substitute

for sodium chloride as a condiment is the production of a characteristic 'saltiness' when employed upon food. Unless the substance is characterized by the taste of sodium chloride, no matter how many other desirable characteristics it may possess, it is worthless as a salt substitute.

Aromatic organic compounds were not considered on account of their toxic nature when used in quantities of four to five grams a day. The physical natures (liquid state, disagreeable odor, etc.) of thousands of aliphatic compounds eliminated these from consideration. The toxic nature of the ions of the heavy metals, the similarity to sodium chloride of many of the compounds of the alkali metals precluded these as possibilities. All inorganic acids and bases were considered unsuited for this purpose. The fact that the agreeable salinity of sodium chloride is dependent upon the chlorine ion, and not the sodium ion, led to the careful consideration of the sodium salts of the acids obtained by mild oxidation of certain carbohydrates, for an acid radical which resembled the chlorine ion in taste. Further, an acid of high molecular weight was considered desirable for this would reduce the percentage of sodium

in the molecule Sodium gluconate, sodium mucate and sodium saccharate were found to be practically useless for this purpose—the tastes of these compounds did not resemble that of sodium chloride. In addition to this, certain investigators<sup>1</sup> have shown the nephrotoxicity of these acids.

The next series of compounds investigated were the fruit acids, most of which are hydroxy acids of the methane series of hydrocarbons. Tartaric and lactic acids salts were not suitable on account of the fact that the former had been shown by Underhill et al.<sup>4</sup> to produce kidney damage and the sodium salt of the latter was not strongly saline. The sodium salt of citric acid was somewhat saline, yet its taste was not nearly so desirable as that of sodium chloride. Sodium citrate presented itself as a possibility in view of the work of Salant and Wise<sup>5</sup> who showed that sodium citrate, when given in reasonably large doses, was not toxic to rabbits. These investigators found only negligible quantities of the sodium citrate in the blood and urine after the ingestion of large quantities of the salt.

In the further study of the fruit acids, malic acid (which is present to the extent of 0.6% in apples) was studied. The sodium salt of this acid was found to have a taste almost identical with that of sodium chloride. After overcoming many of the difficulties of drying the syrupy mass obtained in the evaporation of solutions of sodium malate, this was mixed with various other materials in varying proportions in order to enhance its salt-like taste. These mixtures contained large percentages of sodium malate,

with small quantities of ammonium and sodium citrates to which about one-half of one per cent of manganese bromide was added. This small quantity of manganese bromide was found desirable to enhance the agreeable salty taste of the mixture. Furthermore, the fact that the halides of manganese are inappreciably ionized made manganese bromide especially suited for the purpose intended. Just as the chemist names the undiscovered elements in the periodic system eka iodine, eka caesium, etc., for convenience, in the laboratory the saline mixture was designated as eka salt.

*Organoleptic Tests* Various sodium malate mixtures were employed on food by healthy individuals in place of sodium chloride as a condiment—the similarity in taste between eka salt and sodium chloride was agreed upon by those using it. Eka salt was placed in the salt shakers on the table in three different homes without the knowledge of the members of the family—these folks used eka salt in place of sodium chloride without becoming aware of the substitution.

In the laboratory triturations were made with eka salt and sodium chloride separately in barium sulphate as a dispersion medium in order to determine the vanishing points of salinity by the organoleptic tests. Eka salt by this method possessed 7/8 the salinity of sodium chloride.

This mixture consisted of 85.5 per cent sodium malate, 9 per cent citrate, 5 per cent ammonium citrate and 0.5% manganese bromide. There is a possibility that in the preparation of the salt that double decomposition ensues

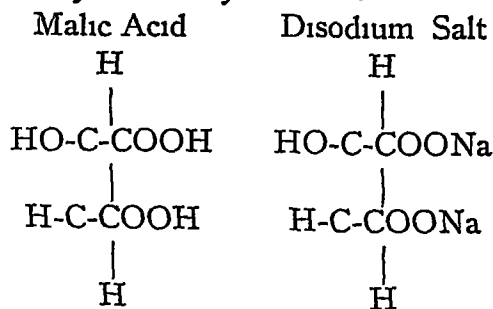


in part between the ammonium citrate and a portion of the sodium malate

#### *Physical Properties of Eka Salt*

Eka salt occurs as a white granular powder, which is readily soluble in its own weight of water. A ten per cent solution of the salt has a pH between 7 and 8, measured by means of the hydrogen-electrode. The specific gravity of eka salt is 1.8, that of sodium chloride is 2.16, i.e., eka salt is 14 per cent less dense than sodium chloride. The osmotic pressure of sodium chloride in 0.1N solution, measured by the depression of the freezing point method, is 4.28 atmospheres, that of eka salt in the same concentration (expressed in grams) is 2.059 atmospheres, i.e., the osmotic pressure of sodium chloride is 108 per cent greater.

*The Chemistry and Metabolism of Eka Salt* Malic acid was isolated first by Scheele in 1785 from green apples. The acid chemically is monohydroxy-dicarboxy-ethane or



The levorotatory compound occurs in nature, whereas the synthetic variety used in the preparation of eka salt is the racemic form. This is synthesized by the catalytic oxidation of benzene by air through maleic acid as described by Downs,<sup>6</sup> Ohta,<sup>7</sup> Wise,<sup>8</sup> Underhill and Pack<sup>9</sup> and Rose<sup>10</sup> have studied the metabolism of salts of malic acid on

various experimental animals and have demonstrated the fact that malic acid in reasonable quantities (10 to 12 Gm to rabbits) is completely metabolized and devoid of toxic action. The amount of malic acid ingested by one using 4 gm of eka salt is equivalent to the amount of malic acid contained in two average sized apples. The same quantity of eka salt introduces into the system about as much citric acid as one would obtain from about one-tenth of a lemon.

The presence of such small quantities of the salts of citric acid and the fact that manganese (0.5% in the form of bromide) has been shown by Baigero<sup>11</sup> to be eliminated in the feces as sulphide, reduces the problem essentially to the study of the metabolism of sodium malate.

*Influence of Eka Salt upon Chloride Elimination* Dogs were fed a diet of milk and biscuit of definite chloride content. The urine was collected daily over five days and the chloride content determined.

TABLE I

Dog No 1	Average NaCl output in 24 hrs 2.44 Gm
Dog No 2	Average NaCl output in 24 hrs 2.51 Gm

Upon the same diet the dogs were fed 5 Gm eka salt daily and over a period of eight days the chloride elimination in the 24-hour specimen of urine was determined.

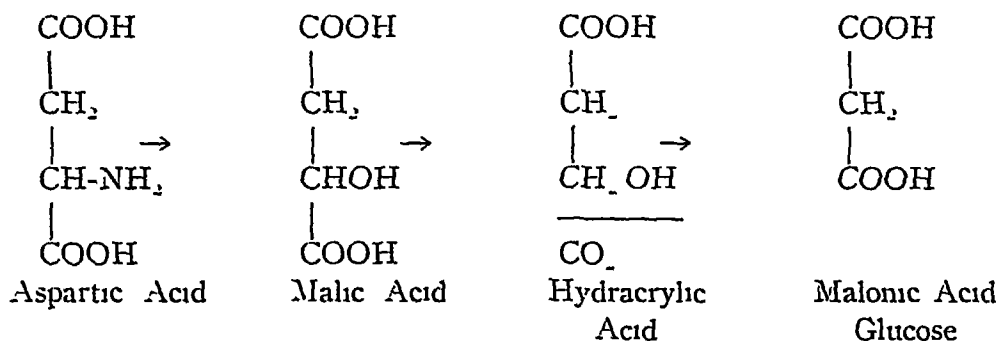
Dog No 1	Average NaCl output in 24 hrs with eka salt 2.28 Gm
Dog No 2	Average NaCl output in 24 hrs with eka salt 3.07 Gm

When the eka salt was replaced by 5 gm of sodium chloride the chloride content of the urine was increased by 76 to 94% of the amount of chloride ingested which appeared in the urine in addition to that chloride from the standard diet

This is indicative of the fact that eka salt when ingested does not cause

an increased chloride elimination by the kidney

*The Fate of Malic Acid* Malic acid is a substance which is not foreign to the human metabolic process when protein is ingested, for it is formed in the metabolism of aspartic acid which is present in most protein bodies Ringer et al<sup>12</sup> have shown the following metabolic changes occur



To confirm this work these investigators demonstrated that malic acid would give rise to extra glucose in phlorhizimized animals

To confirm this work in man, an individual was fed 4 gm of Eka salt daily for five days and the usual twenty-four hour urine specimens collected and examined qualitatively for malic acid. The author was unable to find malic acid in the urine indicating its catabolism as previously suggested

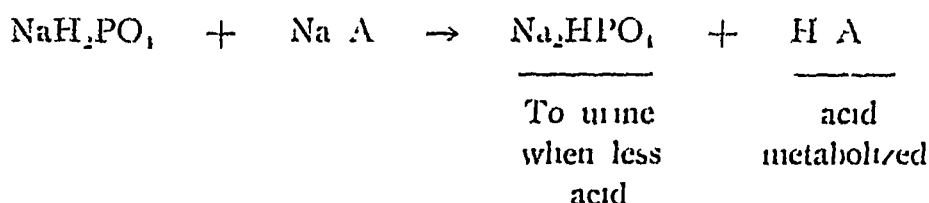
The urine was examined for malic acid as follows. Evaporate 10 c c of acidified urine to dryness, extract the residue twice with 15 c c of boiling ether. Evaporate the ethereal extractions to dryness and add 1 c c of a freshly prepared solution of beta naphthol 0.1 Gm in 5 c c of concentrated sulphuric acid<sup>13</sup>. Warm over a water-bath for 30 to 60 seconds and then add 10 c c of water. In the presence

of malic acid (which is extracted by the ether) a yellow color develops which fades upon standing. With urine the test was found sensitive to 1 mgm of malic acid in 1 c c

This experiment would seem to indicate that in the ingestion of 4 gm of eka salt, the maximum quantity generally employed as a condiment, the malic acid present would be completely metabolized

*The Fate of Sodium* The ideal substitute for sodium chloride in the diets of salt restriction would be one that contained no metallic ion at all. The present author was unable to find such a substance, but in the composition of sodium malate this objection is reduced to a minimum. In the ingestion of sodium malate (after the metabolism of the malate radical) the sodium atom would at first add to the alkali reserve of the blood and be com-

pensated by the acids arising during the normal metabolism of proteins. It is therefore likely that the excretion of the alkali takes place as follows



view of the metabolism of eka salt a normal individual was placed on a diet of reasonable uniformity and twenty-four-hour specimens of the urine collected and the nitrogen, phosphorus and hydrogen-ion determinations were made. The nitrogen and phosphorus were determined by the well-recognized methods and the hydrogen-ion determination made by the electrometric method using a Wilson electrode.<sup>15</sup> Table II gives the results of these determinations.

From Table II it was determined that the average total nitrogen eliminated in twenty-four hours without eka salt was 8.55 gm. Over the same number of days with eka salt the average nitrogen elimination in 24 hours was 8.39 gm. The average phosphorus elimination estimated as P<sub>2</sub>O<sub>5</sub> without eka salt was 1.88 gm., with eka salt the average elimination was 1.90 gm. P<sub>2</sub>O<sub>5</sub>. These results indicate that the ingestion of eka salt in this amount does not influence the nitrogen or phosphorus elimination.

A very significant change in the pH of the urine can be readily observed from the table. The ability to replicate this change on the same individual is of special interest. The arith-

This reduction of urine acidity under similar conditions was studied by Underhill and Wakeman.<sup>11</sup>

To substantiate the validity of this

metric average of the pH determinations of the urine without eka salt is pH 5.97—with eka salt the average pH is 6.96. Determining the Probable Error in this series of determinations according to the formula

$$P.E. = 0.8453 \times \frac{\sum D}{N}$$

where D is the average deviation and N the number of observations, the Probable Error in the case of the observations made without eka salt is 0.26 pH or 4.4% and with the observations made with eka salt the Probable Error is 0.24 pH or 3.51%.

The influence of eka salt upon the acid-base equilibrium of the urine is readily seen in graph No. 1.

The decreased acidity of the urine seems to be desirable in nephritis, Fischer<sup>10</sup> claims the presence of acid in the urine favors the solution of kidney colloids and may produce albuminuria. This investigator contends also that base-yielding foods are desirable in nephritis. Eka salt serves as a base-yielding condiment.

*Sodium-Ion Elimination.* In restricting salt from the diet of the nephritic the physician is interested usually in reducing the number of particles (ions and undissociated mole-

\*Where HA represents malic acid.

TABLE II  
EKA SALT METABOLISM

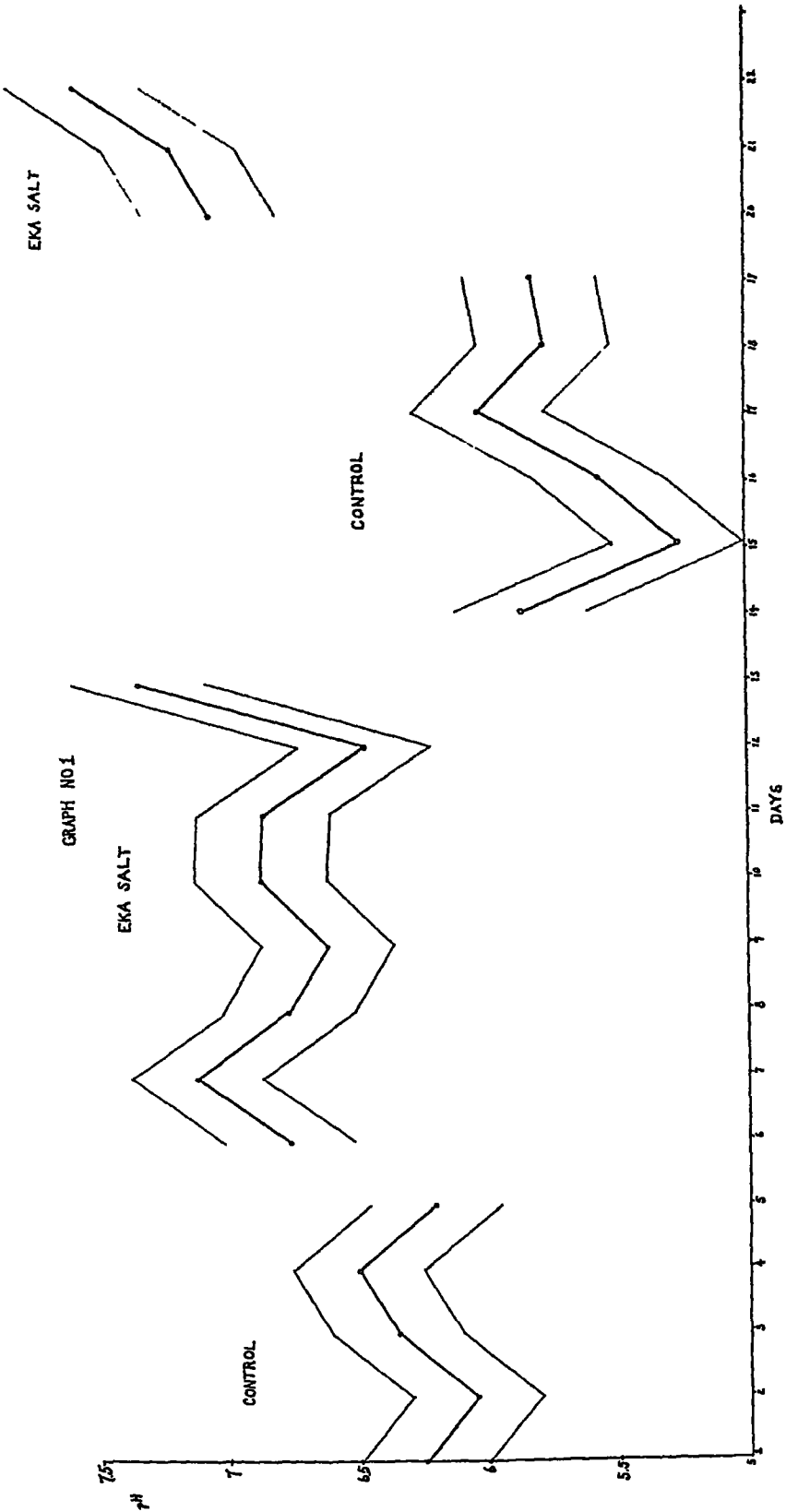
Date	Volume in cc	pH	gm of $P_2O_5$ in 24 hrs	% $P_2O_5$	gm of $N_2$ in 24 hrs	% $N_2$
No Eka 2/14/29	650	6.26	1.76	0.271	6.92	1.06
No Eka 2/15/29	730	6.08	1.63	0.219	8.03	1.10
No Eka 2/17/29	820	6.36	1.83	0.223	7.98	0.97
No Eka 2/18/29	925	6.50	1.85	0.202	6.99	0.76
No Eka 2/19/29	710	6.21	1.94	0.273	8.37	1.15
Eka 2/21/29	810	6.75	1.81	0.224	6.23	0.77
Eka 2/22/29	950	7.27	1.50	0.158	7.11	0.75
Eka T/23/29	1030	6.75	2.26	0.220	8.08	0.78
Eka 2/24/29	1290	6.61	2.60	0.202	11.01	0.85
Eka 2/25/29	810	6.85	2.07	0.256	8.39	1.04
Eka 2/26/29	780	6.84	1.63	0.210	8.03	1.03
Eka 2/27/29	900	6.47	2.20	0.234	11.03	1.23
Eka 2/28/29	875	7.30	1.33	0.164	8.88	1.02
No Eka 3/ 1/29	785	5.85	2.15	0.271	9.73	1.24
No Eka 3/ 2/29	720	5.24	2.11	0.294	10.13	1.41
No Eka 3/ 3/29	700	5.58	1.84	0.264	9.41	1.34
No Eka 3/ 4/29	750	6.03	1.78	0.238	8.35	1.11
No Eka 3/ 5/29	535	5.75	1.85	0.346	8.28	1.55
No Eka 3/ 6/29	775	5.81	1.93	0.250	9.93	1.28
Eka 3/ 7/29	1,140	7.08	2.07	0.182	7.82	0.69
Eka 3/ 8/29	960	7.18	2.07	0.216	6.79	0.71
Eka 3/ 9/29	615	7.52	1.32	0.218	9.01	0.93

cules) necessary for the impaired organ to eliminate. With eka salt there is no increased chlorine-ion elimination and the elimination of the sodium-ion ingested based upon the above experiments reduces itself to a definite mathematical basis.

Eka salt contains 24.4 per cent of

sodium (Na). The ingestion of 4 gm therefore results in  $4 \times 0.244 = 0.976$  gm Na. To supply this amount of sodium from NaCl would require  $NaCl = 58.4$  and  $Na = 23$ .

$\frac{58.4}{23} = 2.5 \times 0.976 = 2.44$  gm NaCl

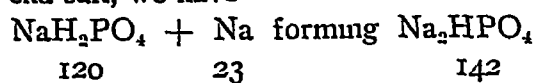


In 0.1 M solution NaCl is 84% ionized. The molarity of a solution of NaCl containing 2.44 gm NaCl is

$$\frac{2.44}{58.4} = 0.0417 \text{ molar}$$

In this concentration assuming ionization 90% complete we have

$0.0417 \times 0.90 = 0.03752$  conc of  $\text{Na}^+$  hence the total  $[\text{Na}^+]$   $[\text{Cl}^-]$  and  $[\text{NaCl}] = 0.0797$  mole particles for kidney elimination when 2.44 gm of NaCl is ingested. Considering now eka salt, we have



From one gram Na approximately 6 gm of  $\text{Na}_2\text{HPO}_4$  result

Expressing in molar concentration, we have

$$\frac{6}{142} = 0.042 \text{ molar}$$

In this concentration disodium phosphate is about 75% ionized. Therefore  $0.042 \times 0.75 = 0.0315$  conc  $\text{Na}^+$  hence the total  $[\text{Na}^+]$   $[\text{HPO}_4^{2-}]$  and  $[\text{Na}_2\text{HPO}_4] = 0.1045$  mole particles for the kidneys to eliminate with 4 gm eka salt containing 0.976 gm Na or approximately 1 gm Na.

But there exists prior to the ingestion of the Na in the eka salt the  $\text{NaH}_2\text{PO}_4$  which would require 0.073 mole for the kidney elimination.

Hence the ingestion of eka salt is responsible for the difference between these values or  $0.1045 - 0.073 = 0.0315$  mole particles added by 4 gm eka salt. Comparing this with NaCl calculated above, when only 2.44 gm

is ingested the  $\text{Na}^+$  and  $\text{Cl}^-$  and NaCl molecules were 0.0797 molar

$$\text{Therefore } \frac{0.0797}{0.0315} = 2.53$$

that is, there are 2.53 per cent more particles eliminated from the Na in the form of NaCl than the same amount of Na in the form of eka salt.

*Clinical Use* During the past year in the hands of several clinicians of this city and its vicinity eka salt has been used as a dietary substitute for table salt in various conditions where a diet of salt restriction was prescribed. In all cases (numbering about 150) the patient found eka salt an adequate dietary substitute for table salt. In no instance did the attending physician report any untoward effects. The results of the clinical findings during the use of this sodium chloride substitute will be reported in a subsequent communication.

#### CONCLUSIONS

- 1 The metabolism of certain sodium malate combinations has been studied.
- 2 A dietary substitute for sodium chloride in the diets of salt restriction has been described.
- 3 Certain advantages of this substance, eka salt which is essentially sodium malate, over sodium chloride in salt-restricted diets have shown experimentally.

Throughout this investigation the author has been indebted to Mr C Jelleff Carr for his technical assistance.

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# Typhoid Fever Complicated By a Perforated Gangrenous Appendix\*

## Report of a Case with Recovery

By MITCHELL BERNSTEIN, M D , *Philadelphia, Pa*

**A**PPENDICITIS complicating typhoid fever is not of frequent occurrence, but failure to recognize this important complication may prove of serious consequence. Statistics reveal the total typhoid fever death rate for seventy-four cities of the United States during 1928 at 1.89 per 100,000 population<sup>1</sup>. Some of these deaths were doubtless due to complications such as perforation and hemorrhage. In addition, appendicitis complicating typhoid fever, unless recognized and properly treated, may end fatally, because of suppuration, perforation, or both.

Previous attacks of appendicitis predispose to an acute flare-up at any time during the course of typhoid fever. The symptoms may be so slight as to escape attention. However, the occurrence of acute pain in the right lower abdomen together with tenderness and spasm of the right lower abdominal muscles, with a temporary fall of the temperature, with or without diarrhea, during the course of typhoid fever, should suggest the possibility of

a complicating appendicitis. An increase in the total number of leukocytes together with a rise in the polymorphonuclear count is of the greatest importance in diagnosis. Shock, which is usually present in perforation, is generally absent. While the appendiceal symptoms occasionally subside, the inflammation may go on to suppuration and lead to final rupture.

The following case report is illustrative of the latter complication. This case would probably have ended fatally and would have been classified as a death due to typhoid fever, were it not for the fact that proper diagnosis and surgical intervention avoided fatality.

*Case report*—On February 6th, 1929, D. H., female, 14 years of age, was admitted to the medical service of Dr. Bernard Kohn, at the Jewish Hospital, complaining of severe headaches and fever. The patient stated that these symptoms had been present for eight days prior to her admission. She had previously been a patient in the hospital, having been there from November 25th, 1928, to January 19th, 1929, with influenza. During this time she was in close association with another patient who had typhoid fever.

\*From the Medical Service of Dr. Bernard Kohn, Jewish Hospital, Philadelphia, Pa.

<sup>1</sup>J. A. M. A., 92 No. 20, pp. 1677, 1929.



On admission the patient's temperature was 103.6°F, the pulse rate was 110, and the respiratory rate was 22 per minute. Her face was flushed. She had an anxious expression. There was no jaundice. The mouth was dry, the tongue was heavily coated, and the breath was foul. Examination of the neck revealed no abnormality. Examination of the chest revealed a left-sided pleural effusion which extended up to the eighth rib posteriorly. (This pleural effusion was present at the time of her previous discharge from the hospital on January 19th, 1929, repeated examinations of the pleural fluid having failed to reveal any evidence of a tuberculous nature.) The breath sounds at the apex of the left lung were slightly exaggerated, the lungs otherwise being apparently normal. The heart was slightly displaced to the right but was normal in size. On auscultation a faint systolic murmur, with transmission to the left axilla, was heard in the fifth left interspace. The blood pressure was 100 mm systolic and 60 mm diastolic. Examination of the abdomen revealed a few scattered rose spots. The abdomen was slightly distended, but there was no tenderness or rigidity. The spleen was not palpable although it was slightly enlarged on percussion. The extremities were negative.

Examination of the urine was negative. A leukocyte count showed 8200 cells with 75% polymorphonuclear, 23% small mononuclear and 2% large mononuclear cells.

On February 8th, two days following admission, the Widal reaction was positive for typhoid fever.

On February 11th, five days following admission, the patient complained of pain in the lower right abdomen associated with vomiting. The abdomen at this time was slightly distended. The leukocyte count showed 8000 cells with 87% polymorphonuclear and 13% small mononuclear cells. The pain and vomiting continued the following day and there was also some diarrhea. There was some rigidity of the lower right abdominal muscles. The next day the pain in the lower right abdomen became unbearable, and there was exquisite tenderness and muscle spasm over this area. Rectal examination revealed tenderness on the right side. The leukocyte count was 11,000 with 87% polymorphonuclear and 13% small mononuclear) and later the same day the blood count showed 14,400 leukocytes and 89% polymorphonuclear with 11% small mononuclear cells. The temperature which had varied from 102° to 104.6°F dropped gradually to 100°F at this time. The pulse rate which had averaged 110 per minute dropped to 90 per minute for a short interval and then continued at the average rate of 120 per minute. A diagnosis of perforated gangrenous appendix complicating typhoid fever was made and confirmed by Dr. William H. Teller, who advised conservative treatment temporarily, consisting of Murphy proctoclysis and heat to the lower right abdomen.

During the following nine days the patient's temperature was of septic type, ranging from 99° to 104.6°F, and the pulse averaged 120 per minute. The tenderness and muscle spasm remained unchanged in the lower right

abdomen and the percussion note over this area was markedly impaired. Rectal examination revealed a bulging mass in the right side.

On February 22nd, 1929, Dr. William H. Teller operated upon the patient and found a perforated gangrenous appendix with secondary involvement of the right fallopian tube. Drainage was necessary. Culture from the pus obtained at operation was negative for typhoid bacilli but positive for colon bacilli. The Widal reaction on February 23rd-24th and later on April 10th remained positive for typhoid fever. The course subsequent to operation was uneventful. The temperature became normal on March 2nd, 1929, eight days following operation, this being the thirty-second day of the illness.

The blood chemistry was constantly normal. Repeated examinations of the urine showed a varying specific gravity from 1.004 to 1.028, no sugar, an occasional trace of albumin and at times a few hyaline casts.

The patient was discharged from the hospital on April 11, 1929, in good condition except for a slight opening of the operative wound which closed completely on July 3rd, 1929, as reported by her physician, Dr. Harold Lipshutz.

*Conclusion* —The case herein reported emphasizes the importance of the recognition of acute appendicitis complicating typhoid fever, and the necessity for proper surgical intervention.

# The Acid-Base Composition of Gastric Juice During the Secretory Cycle\*

By THEODORE L. BLISS, M.D., *Fellow in Medicine,  
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MANY determinations have been made of the acids and the total chlorides in the gastric secretion, but only a few of the other inorganic constituents. All observers have found that there is an increase in the concentration of the total acid and free hydrochloric acid in the normal gastric secretion following stimulation. However, observers have found differences in the response of the chlorides to stimulation. Berglund, Wahlquist and Sherwood found that the concentration of chlorides was essentially equal to that of the hydrochloric acid titrated in the secretion from a human subject having an acidity range within normal limits, after stimulation by histamine. They concluded that such a gastric juice contained little, if any, chloride in combination other than with hydrochloric acid. Bulger and Allen, and Bulger, Stroud and Heideman found that the concentration of chloride did not vary markedly in mixed gastric secretion after stimulation by a water meal, and concluded that chlorides were secreted

into the stomach at a rate which was practically constant. Gamble and McIver obtained similar results in the secretion from pouches of the fundus of cats, using various types of food for stimulation, and drew the same conclusions. Pollard, Roberts and Bloomfield, on the other hand, found that the concentration of chloride promptly increased in mixed gastric secretion of human beings after stimulation with histamine to a maximum which occurred at the same time as the maximal concentration of acid. Later in the cycle, the concentration of the acid tended to fall more quickly, whereas that of the chloride fell slowly. They also found that the concentration of chloride exceeded the concentration of the hydrochloric acid titrated, and believed that some of the chloride was combined in other forms. This excess of chloride was largely accounted for by base. They calculated the total chloride output in the various phases of the gastric cycle on the basis of the volume of the secretion recovered in each phase. This showed an absolute increase in the output of chloride which did not correspond to the respective increase in concentration in the majority of cases. They believed this indicated that at a

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given concentration the actual amount of chloride secreted may vary considerably. Close found that the concentration of chloride in a mixed secretion varied in the same manner as the concentration of the free hydrochloric acid after stimulation with histamine, the former always exceeding the latter.

If this excess of chloride over the concentration of free hydrochloric acid under these conditions is evidence of the presence of inorganic chloride in the gastric juice, it may be used as an approximate index of the amount of inorganic base present. Only a few observers have determined the total base in gastric secretion directly. Rosemann determined the sodium, potassium, calcium and magnesium in pooled specimens of a mixed secretion from the pylorus and fundus of a dog after stimulation with food through an operative esophageal fistula, and from them calculated the total base. More recently, Gamble and McIver determined the total base in the secretion from isolated pouches of the pylorus and fundus of dogs, the secretion was collected at various intervals following stimulation with different types of food. Bulger, Stroud and Heideman used a water meal to stimulate gastric secretion in human subjects, and determined the total base in it after correction for the volume of the water meal. Pollard, Roberts and Bloomfield determined the base in mixed gastric secretion of human subjects collected fractionally after stimulation with histamine. They also calculated the output of base in each period of the gastric cycle on the basis of the volume of secretion which was recov-

ered. Close determined the total base in such secretion, and in the secretion from the Pavlov pouch of a dog, both of which had been collected fractionally after stimulation with histamine. These investigators obtained essentially the same results. They all found that the concentration of base in the fasting content was greatest in cases of achlorhydria and lowest in the cases of hyperchlorhydria. After stimulation the concentration of base decreased as the concentration of free hydrochloric acid increased, the relative degrees of variation in each being roughly proportional. Close further found that the concentration of base was increased after stimulation, in four cases of achlorhydria, but did not proffer an explanation. Pollard, Roberts and Bloomfield found that the actual amount of base, as compared to the concentration values, was increased after stimulation so that it varied in the same manner as the free hydrochloric acid. They believed this indicated that stimulation resulted in the activity of all types of gastric secretory cells. So far as I know, Rosemann alone has determined the constituents of gastric base. Gamble and McIver determined the potassium and calcium and calculated the sodium by subtracting the sum of the potassium and calcium from the total base. They disregarded the magnesium, since Rosemann had found it present in such small amounts.

This report deals with determinations of the acid titrated, the chloride, the fixed base and its various constituent cations, sodium, potassium, calcium and magnesium, in the fasting gastric content, and their changes dur-

ing the successive periods of the gastric secretory cycle following gastric stimulation with histamine

#### METHOD OF EXPERIMENT

The gastric secretion in these experiments was collected from two healthy laboratory workers, from one patient, and from a dog with a Pavlov pouch. The human subjects were fasted for fourteen hours previous to the intubation, and were urged to minimize the amount of saliva swallowed for several hours prior to, and during, the experiment. The usual Rehfuß tube was passed and the stomach emptied as completely as possible by gentle aspiration. This material has been taken to represent the fasting content. Then 0.1 mg of histamine was given hypodermically and the resultant secretion aspirated as completely as possible at the end of each fifteen-minute interval for one hour, at which time the gastric cycle was deemed to be essentially completed. In two instances, continuous aspiration was attempted by means of siphonage, in an effort to recover the entire secretion in each phase of the cycle. The presence of grossly visible bile was taken as an index of duodenal regurgitation and when it appeared the experiment was terminated forthwith. Bile was not grossly visible in any of the experiments presented here. The amount of histamine used did not in any instance cause an untoward reaction. Similar experiments were carried out on a dog with a Pavlov pouch. This afforded a secretion from the fundus rather than a mixed secretion, but one which was not contaminated by saliva or regurgitated duodenal contents. The

dog was fasted for fourteen hours, then the pouch was drained for one hour and the material was taken to represent the fasting content. Since it had been shown that larger doses of histamine prolonged the secretory phase rather than increased the intensity of the response, 0.5 mg was used in the dog to obtain sufficient material for analysis. The secretion was collected in one hour periods for four hours, at which time the acid concentration was well in the diminishing phase. The collections were repeated on successive days and the corresponding samples pooled until sufficient material for analysis was obtained. The effect of bacterial activity was minimized by keeping the material on ice until analyzed.

The individual samples were measured and then filtered through several thicknesses of gauze. On the filtrate the free hydrochloric acid was titrated with tenth-normal sodium hydroxide, using Topfer's reagent as the indicator, and the total acidity was titrated with tenth-normal sodium hydroxide, using phenolphthalein as the indicator. The total chlorides were determined by the Harvey modification of the Volhard method. Preliminary analysis indicated that the mucin in this filtrate interfered with the direct precipitation of the various inorganic cations present. Therefore, the mucin was removed by "shaking out" with well washed chloroform. This was found to be the simplest and most satisfactory method of preparing the sample for subsequent analysis. The total base was then determined by the Fiske method, the sodium by the modified Kramer and Tisdall method on an

aliquot portion, the hydrogen-ion concentration of which had been adjusted to pH 7.1 with alcohol-washed potassium hydroxide; the potassium by the Kramer and Tisdall method on an aliquot portion, the hydrogen-ion concentration of which had been adjusted to pH 5.6 with sodium hydroxide, and the calcium by the Clark-Collip modification of the Kramer and Tisdall method on an aliquot portion, the hydrogen-ion concentration of which had been adjusted to pH 5.4 with ammonium hydroxide. Preliminary analyses revealed that magnesium was present in so small an amount, and varied so little during the gastric cycle, that it constituted a negligible fraction of the total base. Hence, it was not determined in the later experiments presented here.

### RESULTS

The determinations of five experiments are presented in the tabulation. In the first two experiments the variation of the free hydrochloric acid during the gastric secretory cycle was within normal limits. The material was obtained from two healthy laboratory workers. In the third experiment the increase in free hydrochloric acid exceeded the normal limit, and represents a curve of hyperchlorhydria. This material was collected on another occasion from the same subject as the material in the second experiment. In the fourth experiment, free hydrochloric acid was absent during all phases of the cycle and represents a curve of achlorhydria. This material was from a female patient who had diabetes of a mild degree, but who did not manifest signs or symptoms of a

gastric lesion or evidence of pernicious anemia. The data of the experiment on the gastric juice from a dog with a Pavlov pouch are given in the fifth experiment. The free hydrochloric acid varied within normal limits in the uncontaminated secretion from the fundus. The data in all the experiments are similarly arranged, and all values are expressed in cubic centimeters of tenth-normal acid or base for each 100 c.c. of secretion, except the amounts of secretion which are expressed in cubic centimeters. In the preliminary analyses, the duplicate determinations of the calcium, the chloride and the acid values agreed so uniformly that the utilization of a single determination was justifiable. The sodium, the potassium and the total base were determined in duplicate, except when material was not sufficient, and their averages are presented in the tabulated experiments. The duplicate analyses agreed within a 3 per cent variation, with the exceptions indicated, and these were within a 5 per cent variation. The sum of the sodium, potassium and calcium determinations are presented as a check on the respective total base. The various inorganic constituents will be considered collectively.

In all the experiments except that with achlorhydria, the curves of the total acid and free hydrochloric acid reacted in a similar manner after stimulation by histamine. During the first part of the cycle the concentration of both increased rapidly, but in varying degrees, to a maximum which occurred thirty minutes after stimulation in the human subject, and two hours after stimulation in the dog. Toward the

end of the cycle the concentration of the total acid and free hydrochloric acid gradually decreased. In the experiment with achlorhydria (fourth experiment) stimulation caused an increase in the concentration of the total acid, which subsequently decreased, but the amount of change was so small that it was inconclusive. There was no secretion of free hydrochloric acid.

Of all the experiments the relative amount and variation in the concentration of the combined acid is striking only in the dog, in whom it constitutes 50 per cent or more of the total acid in every phase of the cycle.

The curve of secretion of chloride was comparable in all the experiments except the achlorhydria. The concentration of chloride was lowest (62 to 113 c.c. of tenth-normal solution for each 100 c.c. of secretion) in the fasting secretion. After stimulation, the concentration of chloride increased to a maximum (87 to 130), which occurred at the same time as the maximal concentration of free hydrochloric acid. Toward the end of the cycle the concentration of chloride decreased. However, the amount of increase or decrease in the chloride was in every instance less than the corresponding increase or decrease in the free hydrochloric acid. In the experiment with achlorhydria, the concentration of chloride was essentially the greatest (115) in the fasting content, it decreased after stimulation to 99. Its variations were in the same direction as the variations in the concentration of total base, but not to an equivalent amount. In comparing the relative levels of concentration of chloride in all the experiments, it would appear

that the level of the concentration of chloride is dependent on the level of the concentration of the respective total cations.

The curve of the secretion of base was comparable in all experiments. The concentration of base was greatest (59 to 142 c.c. of tenth-normal base for each 100 c.c. of secretion) in the gastric content of the fasting subject. After stimulation the concentration of base decreased in each experiment to a minimum (38 to 90) which occurred approximately at the height of the acid response. Later in the cycle the concentration of base was increased. However, the amount of variation in the concentration of base was not equivalent to the respective amount of variation in free hydrochloric acid, if it was present. A comparison of the fasting levels of concentration of base in the various experiments revealed that it was greatest in achlorhydria (142) and lowest in hyperchlorhydria (59). In the mixed secretion from human subjects with a normal acidity the fasting concentration of total base (78 and 80) was slightly less than it was in the secretion from the fundus of the dog (90). It would seem that the relative concentration of total base in the fasting content was inversely proportional to the concentration of free hydrochloric acid.

Sodium was found to be the most significant of the total base cations, both in amount and in variation during the cycle. In the gastric content of the fasting human subject it comprised between 63 and 73 per cent of the total base in these experiments. In the gastric content of the fasting

dog, sodium constituted 85 per cent of the total base. After stimulation the sodium varied in the same manner as the total base, and its changes, in fact, were approximately the changes of the total base, as they constituted roughly 90 per cent of the changes in the latter.

Potassium was found to be less important in amount and in variation. In the mixed gastric content of the fasting human subject it comprised between 21 and 28 per cent of the total base. In the content of the fundus of the fasting dog it constituted only 10 per cent of the total base. Following stimulation the potassium curve differed in the various experiments. In the second, fourth and fifth experiments it varied in the same manner as the total base, but its variations, as compared with those of sodium, were much less. In the third experiment (with hyperchlorhydria) the concentration of potassium increased so that the curve was the inverse of the base curve, but its total variation was small, whereas in the first experiment, the potassium changes did not form a significant curve.

Calcium was found to be the least significant of the cations studied in these experiments. Its concentration in the content of the fasting stomach in all the experiments was approximately the same, varying from 2.9 to 3.4 c.c. After stimulation its changes in each experiment were in the same manner as the changes in the total base, but the degree of change was too small to be significant.

In comparing the concentration values of those ions common to blood serum and gastric juice it is seen that

the concentration of sodium in mixed gastric juice never comes to within more than 60 per cent of its concentration in the blood serum. The concentration of calcium in a mixed gastric juice is practically the same as the concentration of the so-called diffusible calcium in blood serum, although it is less than the concentration of total calcium. On the other hand, the concentration of potassium in a mixed gastric juice is four times its concentration in serum. The concentration of chloride in a mixed gastric juice at the height of the acid secretion approaches, and in the hyperchlorhydria slightly exceeds, its concentration in blood serum. Thus, in these experiments potassium was essentially the only electrolyte that had a greater concentration in mixed gastric secretion from the human subject than in blood serum. Under these conditions it would appear that there is an active secretion of potassium into the stomach.

In figure 1 the known ions of the second experiment are plotted fractionally in an arbitrary manner. They are plotted on a line above which is acid and below which is base. The cations are in the left half and anions in the right half of the double columns. The cations are the total hydrogen ions plus the total base ions, and can be plotted accurately. The anions include the total chloride ion as determined and the unknown organic combined acid ion as titrated. The anions are arranged so that the chloride is in combination with the hydrogen of the free hydrochloric acid, when it is present. Any excess of chloride is placed in combination with the total base. When



DATA ON GASTRIC SECRETION FROM HUMAN SUBJECTS AND A DOG WITH A PAVLOV POUCH

		Cc tenth-normal acid or base for each 100 cc of secretion									
		Amount, cc	Free hydro- chloric acid	Combined acid	Total acid	Total chloride	Total base	Sum of sodium potassium and calcium	Sodium	Potassium	Calcium
First experiment, normal mixed secretion (human subject)	Fasting		0	10	10	62	79.6	79.0	56.5	19.6	2.9
	After histamine 15 minutes		10	16	26	70	63.8	68.0	44.4	21.0	2.6
	30 minutes		44	20	64	87	45.3	48.6	26.9	19.7	2.0
	45 minutes		38	14	52	79	39.2*	43.1	22.1*	18.9	2.1
	60 minutes		34	16	50	76	43.0	44.4	21.3	20.8	2.3
Second experiment, normal mixed secretion (human subject)	Fasting	16	0	18	18	62	77.5	80.0	56.7	20.8	2.5
	After histamine 15 minutes	41	45	14	59	99	57.5	56.6	33.6	20.7	2.3
	30 minutes	35	54	16	70	101	43.7	46.3	27.1	17.0	2.2
	45 minutes	41	43	15	58	93	47.5	51.9	29.7	19.8	2.4
	60 minutes	30	32	16	48	85	62.5	59.5	35.2	21.7	2.6
Third experiment, mixed secretion in hyperchlorhydria (human subject)	Fasting		37	23	60	85	58.8	59.9	39.8	17.0	3.1
	After histamine 15 minutes		44	21	65	106	61.6*	65.3	42.0	19.8	3.5
	30 minutes		85	21	106	125	37.7*			21.0	2.1
	45 minutes		78	19	97	114	38.8	41.4	20.0**	19.4	2.0
	60 minutes		46	15	61	89	45.6	47.6	26.3	18.4	2.9

Fourth experiment, mixed secretion in achlorhydria (human subject)	Fasting	35	0	5	5	115	142.5	124.1	90.5	30.0	3.6
	After histamine 15 minutes	38	0	7		118	127.5	124.7	96.3	25.3	3.1
	30 minutes	40	0	7	7	104	103.7	101.1	72.7	25.4	3.0
	45 minutes	32	0	5	5	99	90.0	98.2	70.7	24.3	3.2
	60 minutes	30	0	5	5	107	107.5	112.0	80.5*	28.3	3.2
Fifth experiment, secretion from fundus (normal dog)	Fasting		19	61	80	113	90.0**	97.0	82.0	11.6	3.4
	After histamine 1 hour		52	62	114	130	75.0	77.4	64.6	9.4	3.4
	2 hours		56	56	112	130	61.0	66.1	53.5	9.2	3.4
	3 hours		32	63	95	124	85.0*		73.7*		
	4 hours		12	74	86	121	97.0*	96.3	81.9*	10.4*	4.0
Blood serum values						120	160.0		150.0	5.0	5.0

\*Single determination only

\*\*Duplicates within 5 per cent variation

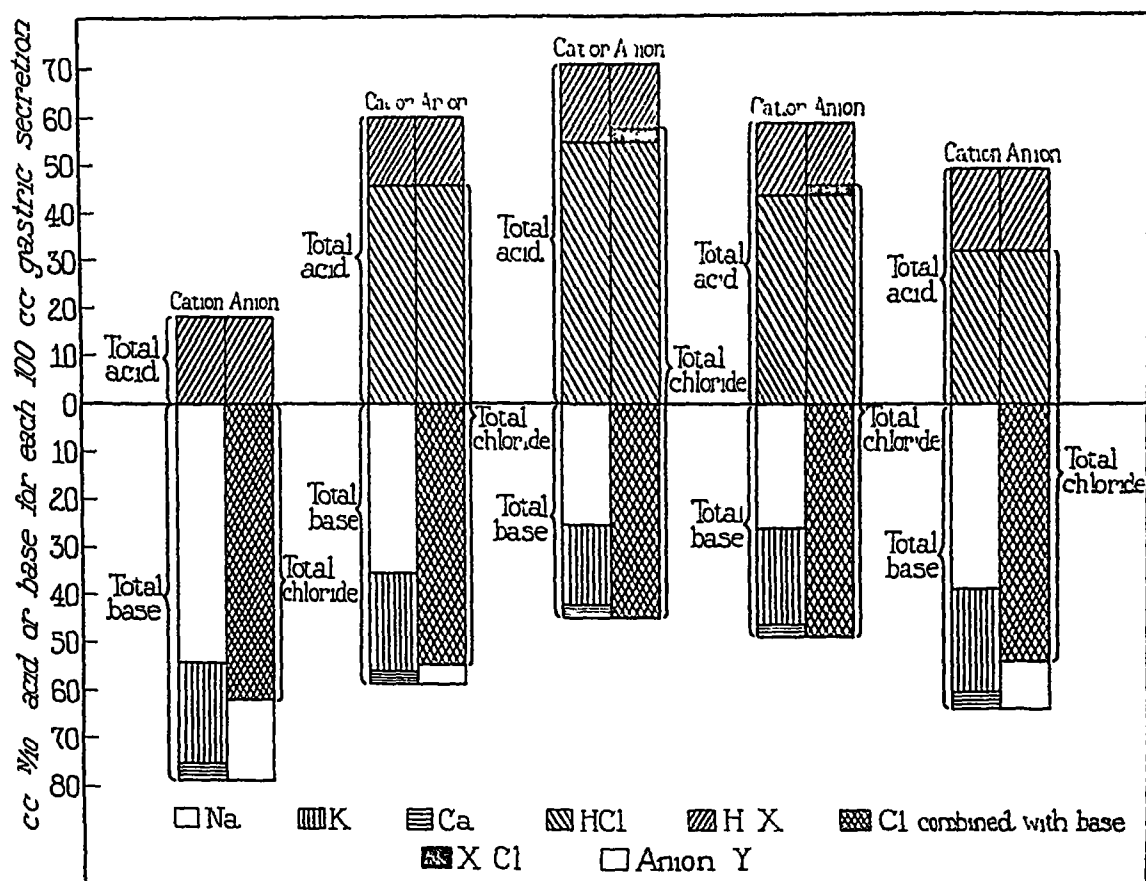


FIG 1 Data of the second experiment The blocks from left to right are the successive phases of the secretory cycle The first represents the fasting secretion, and the next four represent the successive fifteen-minute intervals after histamine stimulation Na, K, and Ca are the cations of the total base H-X is the combined acid as determined by the difference between the titration with phenolphthalein and the titration with Topfer's reagent X represents the unknown anion of the combined acid HCl is the free hydrochloric acid, determined by titration with Topfer's reagent Cl combined with base is shown as the difference between the total chloride and the chloride combined in free hydrochloric acid Anion Y is an undetermined anion and is the difference between the total base and the chloride in combination with base X-Cl is the chloride which exceeds the equivalent of the sum of the total base and the free hydrochloric acid, and is shown in combination with combined acid

there is more chloride than the sum of that combined with free hydrochloric acid and with total base, it is placed in combination with the combined acid anion When the sum of the free hydrochloric acid and the total base is greater than the total chloride, the excess of base is combined with an undetermined anion This anion may possibly be sulphate, phosphate, carbonate, proteinate or an organic anion At the height of nor-

mal gastric secretion the difference between the total cations (hydrogen and base) and the measured anions (total chloride and combined acid anion) is between plus or minus 35 cc of tenth-normal solution for each 100 cc of the mixed secretion This is a value which is well within the limits of the experimental errors of the various analytical method During the fasting period the undetermined anion in combination with base (anion Y) is

relatively larger in amount (15.5 c.c. of tenth-normal solution for each 100 c.c.) and is greater than the summation of probable experimental errors. At the end of the cycle the fasting state is approached. This would seem to indicate that after stimulation in the normal stomach, anions other than chloride ions were not present, except the unknown organic anion in combination with combined acid, whereas they are present in the fasting secretion.

#### COMMENT

All observers agree, in the main, as to the changes in the concentration of the free hydrochloric acid and the total acid of gastric juice that occur after gastric stimulation. Dobson, Pollard, Roberts and Bloomfield, and Close found that the maximal concentration of free hydrochloric acid occurs about thirty minutes after stimulation with histamine in 0.1 mg. doses, except in cases of true achlorhydria. Dobson and Close showed that larger doses of histamine prolonged the secretory response rather than increasing its intensity. These observations have been substantiated in the experiments reported here.

However, the changes in the concentration of total chlorides after stimulation have not been found to be the same by various observers, as has been pointed out. In all the experiments, except the achlorhydria, the concentration of total chloride definitely increased after gastric stimulation to a maximum which occurred at the same time as the maximal concentration of free hydrochloric acid, and then decreased as the concentration of acid decreased. In all instances the con-

centration of chloride exceeded the concentration of free hydrochloric acid, which would indicate that chloride is secreted into the stomach in forms other than hydrochloric acid. In the experiment with achlorhydria the concentration of chloride decreased, its variations roughly paralleled the variation in the concentration of sodium.

The values for concentration of total base in these experiments have been presented. With one exception, they are in accord with the observations on the fractional curve of Pollard, Roberts and Bloomfield, and Close. Whereas Close found an increase in the concentration of base after stimulation in four cases of achlorhydria, I found a definite decrease in the case which I observed. Following the report of Pollard, Roberts and Bloomfield, I attempted, in two experiments, to recover all the gastric juice secreted in each period of the gastric cycle (second and fourth experiments). The calculated total output of base in the normal secretion of the human subject during the gastric cycle in the second experiment gave a curve which approached theirs. In the fasting period 16 c.c. of secretion was recovered, and in the four successive fifteen-minute periods after stimulation by histamine, 41, 35, 41, and 30 c.c. of secretion were recovered respectively. This gave a total amount of 124 c.c. of tenth-normal base in the fasting content, and 236, 153, 195 and 188 c.c. of tenth-normal base in the successive periods of the gastric cycle after stimulation. That only 35 c.c. of secretion was recovered at the height of the acid curve (that is,

in the second fifteen-minute period) probably accounts for the observation that the maximal output of base did not attend the maximal output of acid. This was probably due to failure to recover the entire secretion in that period. It gives a clear indication of the error which such a failure would induce, and shows that the procedure at best has its pitfalls. However, it is fairly definite in this experiment that there is an actual increase in the output of total base after stimulation. In the case of achlorhydria (fourth experiment), the volume of secretion formed a more uniform curve. In the fasting period 35 c.c. of secretion was recovered and after stimulation by histamine 38, 40, 32, and 30 c.c. of secretion were recovered in the respective fifteen-minute periods. The total output of base in the respective periods was 49.9, 48.5, 41.5, 38.8, and 32.3 c.c. of tenth-normal base. Thus, in the experiment with achlorhydria, the total output of base as well as the concentration of base was decreased after stimulation by histamine. The significance of this observation is still obscure.

Complete fractionation of the total base in gastric secretion, during the successive phases after stimulation, seemingly has not been reported heretofore. The values for concentration of sodium, potassium and calcium during the gastric cycle have been given. When calculated in actual amount of each that are secreted in the second and fourth experiments, they are found to vary in the same manner as the total base in their respective experiments. The sodium has been accurately determined and in these ex-

periments it is unquestionably the most significant of the gastric bases. Potassium is second in importance, whereas calcium is relatively of no significance, and magnesium may be disregarded.

Various workers have calculated the unknown amount of various electrolytes from the determined values of other electrolytes. After Gamble and McIver determined the phosphate and protein in samples of gastric juice and found them in negligible amounts as compared with the chloride anion, they believed that the concentration of hydrogen ions is approximately equal to the difference between the chloride ion and the fixed base. This was found to be true in the experiments reported here. Berglund, Wahlquist and Sherwood found that after stimulation the total chloride corresponded approximately to the hydrochloric acid titrated. This was not found to be true in my experiments. Pollard, Roberts and Bloomfield compared the determined gastric acidity with the acidity as calculated by subtracting the base from the total chloride. They found the determined free hydrochloric acid to be greater than the calculated free hydrochloric acid in the fasting content, and attributed this to the absence of free hydrochloric acid. After stimulation the calculated free hydrochloric acid was uniformly higher than the determined free hydrochloric acid, the difference between them not being completely accounted for by base, although the discrepancy was not great.

This is essentially a statement that in the fasting content there is an excess of base over the chloride combined with base, and would indicate

that an anion other than chloride is in combination with base. After stimulation there is not enough chloride to account for both the free hydrochloric acid and the base although the discrepancy is not large, and would indicate that the base is entirely combined with chloride. This was found to be essentially true in these experiments. Close calculated the amount of base chloride by subtracting the total acid from the total chloride and found that its concentration was greater in the fasting content than at the height of the secretory response. This calculation is made but I have calculated the base chloride as the difference between the total chloride and the free hydrochloric acid.

#### SUMMARY

Determinations of the acid-base composition of gastric juice during the secretory cycle in human beings and in one dog have been presented. Data from subjects illustrative of the

changes in normal, hyperchlorhydric, and achlorhydric states have been given.

The concentration of chloride was found to be increased after stimulation except in the achlorhydric state, but in amounts which were less than the increase in the concentration of free hydrochloric acid.

During the secretory cycle the concentration of base varied inversely to the concentration of acid.

Sodium was found to be the most significant of the individual bases, both in regard to its amount, and in regard to its relationship to the variation in the total base during the secretory cycle.

The concentration of the determined ions was found to be less in the stomach than in blood serum, with the exception of potassium. The concentration of potassium was from three to five times greater in the gastric juice than in the blood serum.

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# Hay Fever

## Its Control Through Efferent Interception

By HIRAM BYRD, M D, *Detroit Michigan\**

**H**AY fever, whether seasonal or non-seasonal, is defined in this connection in terms of excess sneezing. Now a sneeze has its conscious origin in the roof of the nose, in a region which without any attempted delineation, may be designated as the "sneeze region."

This sneeze region receives its nerve supply from two branches of the trigeminal—from the superior maxillary, via Meckel's ganglion, and from the ophthalmic, via the nasal nerve. Therefore efferent impulses routed down the trigeminal nerve may reach the sneeze region via either the ophthalmic or the superior maxillary. And since this may occur on either side without involving the other, it is obvious that *there are four routes via which such efferent impulses may reach the sneeze region*.

As will be shown later, there are ample grounds for formulating the hypothesis that the *sneezes are engendered by efferent impulses in excess*. Now if sneezing is engendered by efferent impulses, registering in the sneeze region, then it is obvious that intercepting these impulses before they reach the sneeze region will effectively prevent the sneezing. Such interception may be accomplished by anesthetizing the

nerves proximal to the sneeze region, which intercepts the passage of nerve impulses or currents temporarily, or by injecting the nerves with alcohol, which interferes with the passing of currents more or less permanently.

Now efferent impulses\* routed to the sneeze region via the ophthalmic nerve have to pass the *nasal nerve*, and those routed via the superior maxillary have to pass *Meckel's ganglion*, at which loci the nerves are anatomically reachable. Therefore, the interception of such currents by anesthetization, or injection, is not an important procedure.

Here then the stage is all set for testing the hypothesis under the most rigidly controlled conditions. For if it be true that excess sneezing is engendered by efferent impulses routed down these four nerves in excess quantum, then all one has to do to arrest the sneezing, *regardless of its antecedent cause*, is to obstruct the four paths of impulses into the sneeze region, which may be done by inject-

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\*It is to be noted that physiology assigns to the maxillary and ophthalmic branches of the trigeminal nerve an exclusively sensory function—an assignment that, in the light of these disclosures, calls for re-examination.

ing the two nasal nerves, and the two Meckel's ganglia, with alcohol

Such injection, moreover, if followed by relief from the sneezing, not only supports the hypothesis, but *provides a ready therapeutic approach for the practical control of hay fever*

It was Sluder who first noted that injecting Meckel's ganglia with alcohol arrests some cases of hay fever but not all. Subsequently one of his followers reported some 43 cases in which he had injected Meckel's ganglia for hay fever, with results ranging all the way from complete and permanent relief on the one hand to little or no benefit on the other. The writer's experience is in harmony with those that have found their way into the literature. In some instances, injecting Meckel's ganglia with alcohol gives immediate, complete, and permanent relief from hay fever. In other instances, the relief is only partial, or absent entirely.

In view of the foregoing consideration, however, this is exactly what is to be expected. For while injecting Meckel's ganglia intercepts impulses routed to the sneeze region via the superior maxillary, it leaves those routed via the ophthalmic nerve quite unobstructed, so as only partially to fulfill the conditions for testing the hypothesis.

It was subsequently noted that hay fever cases who had experienced partial but not complete relief from injecting Meckel's ganglia, uniformly exhibited a distinct rhinitis in the anterior portion of the nasal chambers corresponding to the region of distribution of the nasal nerves. Sometimes this anterior rhinitis, it was noted, was

limited to one side, and in such cases, it was further noted, the sneezes had their conscious origin in the affected side. The thought was compelling that in these cases, after Meckel's ganglia had been injected, there was still quite a sufficiency of current coming down the nasal nerve to continue the symptoms. Thus, in order to fully test the hypothesis, we were face to face with the problem of injecting the nasal nerves.

The nasal nerves, however, so far as the writer was able to find, had never been injected with alcohol. And since such injection would have to be made in such close proximity to the cribriform plate, and the olfactory distribution, it was not undertaken without due consideration.

In the meantime another device was resorted to. A case presented in the person of a nurse who had had non-seasonal hay fever from childhood with seasonal exacerbations. Meckel's ganglia were injected as the first step. This was found to give ten days' relief, after which the sneezing returned, though somewhat modified in severity. Moreover, the conscious origin of the sneeze now appeared to be limited to one side.

The region of the nasal nerve on that side was now cauterized with 40% solution of silver nitrate. While this had the effect of arresting the sneezing, the line of approach was too severe, and was accordingly abandoned.

A case now presented with non-seasonal hay fever of three years' duration—a very aggravated case. Meckel's ganglia were injected as the first step, whereupon the hay fever ceased for a period of twenty days, and when it re-



turned, as in the preceding case, the conscious origin of the sneezes appeared to be limited to one side

It was now decided to undertake the injection of the nasal \*\* nerve of this side with alcohol. To this end an applicator was passed into the region, and X-rayed in place, so as to serve as a guide in finding one's way. With these precautions, the injection was made, with the result that all symptoms of hay fever were immediately arrested. Not had there been any recurrence at last accounts, some fifteen months afterward.

In this test then, which has since been verified in both seasonal and non-seasonal hay fever, all evidence goes to support the hypothesis that whatever the antecedent cause of the sneeze may be, its immediate cause is something that travels along the nerves, and which does not have the power to pass a section that is anesthetized or injected with alcohol.

But associated with the sneezes of hay fever are other symptoms, as weeping of the nose and eyes, and particularly burning and itching of the eyes. These associate symptoms are uniformly arrested simultaneously with the sneezing, so that the evidence that goes to establish efferent impulses as an obligate factor in sneezing, similarly establishes such impulses

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\*\*Later developments have disclosed that injecting the nasal nerves at a more proximal point, that is through the orbit, at the point just proximal to the anterior ethmoidal foramen, is a much more dynamic procedure, and is, in itself, often quite sufficient to relieve the hay fever or hyperesthetic rhinitis without recourse to injecting the sphenopalatine ganglia.

as an obligate factor in the associate symptoms. Here then we must conclude that not only the sneezing, but the whole train of associate symptoms, with or without the sneezing, is similarly engendered by excess efferent impulses, and subject to the same methods of control. Let us now see what evidence we have that these associate symptoms, when they appear as entities apart from hay fever, come under the same control.

A case of seasonal itching and burning of the eyes, very similar to that associated with hay fever, but without the sneezing, was found to be temporarily arrestible by anesthetizing Meckel's ganglia. This procedure was repeated several times, with uniform results, but the symptom persistently returned. At length the ganglia were injected with alcohol under general anesthesia. The patient awoke free from the eye distress, which at last accounts had never returned.

Similarly, an aggravated case of rhinorrhea, but without sneezing, presented for treatment. It was found that anesthetizing Meckel's ganglia gave temporary relief from the rhinorrhea, whereupon the ganglia were injected with alcohol. This gave complete relief for a few days, after which the rhinorrhea returned, but limited to the left side, and to the anterior portion of the nose. The left nasal nerve was now injected with alcohol, whereupon the rhinorrhea ceased altogether.

Again, a case of enlarged tonsils, hypertrophic turbinates, and "red-nose," but without sneezing, presented for treatment. It was elected to inject Meckel's ganglion on one side, leaving

the other for control purposes. Following the injection the tonsil on the injected side shrank to half the size of its fellow, the turbinates on that side underwent pronounced regression, and that side of the nose assumed its normal color and texture, while conditions on the opposite side remained unchanged.

Thus would it seem that the sneezing and the other symptoms associated with hay fever are so many separate entities, but all underlain with the same actuating cause, and all amenable to the same therapeutic approach—intercepting the passage of efferent currents into the affected loci.

Re-classifying these several symptoms the evidence is that efferent impulses in excess quantum engender:

“Sensory dys-functions,” as the itching and burning of the eyes,

“Motor dys-function,” as the muscular activity involved in the act of sneezing,

“Respiratory dys-functions,” as the sneeze itself, and

“Secretory dys-functions,” as the rhinorrhea and the lachrymation.

Moreover, and this is important, it is only a step from itching of the eyes to itching of the ears, to pruritus vulvae, and to other sensory manifestations, as arthritis, lumbago, gout, sciatica, etc., all of which have been repeatedly relieved by anesthetizing the nerves along the intervening efferent path. It is only a step from the motor dys-function involved in the act of sneezing to the motor dys-functions of chorea and these too have been immediately and repeatedly relieved by anesthetizing the nerves along the intervening efferent path. It is only a

step from hay fever to asthma, and that too has similarly been relieved. Finally it is only a step from the secretory dys-functions involved in the rhinorrhea and lachrymation of hay fever to the secretory dys-function involved in diarrhoea, and that too has been immediately relieved by anesthetizing the intervening efferent path.

So we must conclude that the arrest of sensory, motor, respiratory, and secretory dys-functions in connection with hay fever, by intercepting the efferent impulses, *involves nothing unique, or restricted to hay fever phenomena, but is indeed merely a part of an underlying principle universal throughout the body*.

Let us now see how far physiology has gone to disclose such a principle. In his recent annual address, Sir Arthur Lovatt Evans, president of the section of physiology of the British Association for the Advancement of Science, said:

“A state of disease is never a thing in itself but is always a quantitative change in some physiological process, an increase or diminution of something that was there to begin with.”

We have it from eminent physiological authority that efferent currents serve to “motivate and stabilize” the various physiological functions. In other words the efferent currents constitute a sort of super-function.

It seems a necessary deduction that there must be limits beyond which the quantitative variations of this super-function cannot go without causing disruption in the functions it normally motivates and stabilizes. This would seem to postulate that efferent cur-

in excess quantum may cause various and remote dys-functions, and that these dys-functions may be arrested by the interception of such currents at any locus along their path

We may now inquire of physiology, is it experimentally known that nerve impulses, or currents, may engender remote dys-functions? and that such dys-functions may be arrested by intercepting the passage of these currents?

Recently the writer was visiting the physiological laboratory of one of the great institutions of the Middle West. On this particular occasion the experimenter had the vidian nerve of a narcotized animal exposed, to which he was applying a stimulus, and noting the results. When the stimulus was applied the respiration, the heart action, and the blood pressure became quite disturbed. When it was withdrawn, these disturbances would subside.

Subsequently the writer wrote to the Director and the Assistant-Director of these laboratories, referring to the incident in the following language:

"As I understand the electrode applied to the nerve caused an impulse, (or succession of impulses, or current or *something*,) to travel along the nerve to some remote locus and *cause* these symptoms. Without raising the question as to the nature of the thing that travels along the nerve, (current, let us call it,) or the mechanism of how it travels, or the mechanism of how it causes these disturbances, or even where it operates to cause them, can't we consider this *current* in its bare essentials as follows. As

originating at the locus of stimulation, as traveling along the nerves, as causing these remote disturbances, and as being unable to pass a section of nerve that is anesthetized, frozen, or injected with alcohol?"

To this question the Director and the Assistant-Director answered separately "Yes."

Having seen that the initiation of remote dys-functions by means of nerve currents is commonplace in the physiological laboratory, let us inquire what evidence the clinic affords on whether the effluent nerve currents of the organism in excess quantum may similarly cause remote dys-functions.

The anatomies show us that Meckel's ganglion is the most important isthmus connecting the largest cranial nerve (the trigeminal) with the sympathetic system. If excess effluent impulses cause remote dys-functions, then in cases where these excess impulses are routed adown the trigeminal nerve and across this isthmus to the sympathetic system, it should be possible, by anesthetization of this isthmus, or injection of it with alcohol, to arrest such dys-functions in regions *distal* to the isthmus, but in no case should it be possible to arrest dys-functions by this procedure in regions of distribution *proximal* to the isthmus.

Now this has actually proven to be the case. Although in more than five hundred cases have remote dys-functions been arrested by anesthetization of Meckel's ganglion in regions distal to it, not one has been found arrestible in regions of distribution proximal to

the ganglion. Thus, upon the hypothesis that efferent currents in excess quantum were the immediate cause of the various dys-functions arrested, the expectations postulated from the anatomical framework are fulfilled in minutest detail.

It may be added that the list of dys-functions thus intercepted includes not merely subjective, but objective disturbances, so that we do not have to rely upon the patient's testimony alone that the symptom has abated. Indeed this fact, together with the immediateness and decisiveness of these reactions, when positive, gives such clinical observations an accuracy comparable only to the controlled experiments of the laboratory.

In summary, the hypothesis that efferent currents in excess quantum are the determining factor, not only in sneezing, but in the other dys-functions associated with hay fever, and indeed with sensory, motor, respiratory, circulatory, and secretory dys-functions throughout the body, is seen to provide us with an interpretation that is at once in harmony with Evans' law, and with the experiments of the

physiological laboratory, and with the anatomy of the structures concerned.

Moreover, this hypothesis, together with the already developed methods of intercepting nerve currents, provides clinical medicine with an instrument of precision in research comparable to the microscope and the test tube in their respective fields—provides a method of investigating sensory phenomena, thus opening to clinical medicine a field of research which, by its very nature, is excluded from the physiological laboratory, where the experimental subject is a dumb narcotized animal.

Moreover *the hypothesis that efferent impulses or currents in excess quantum cause remote dys-functions*, provides a thought formula which, so far, has served as an unerring guide in predicating what may be expected in untried situations. And growing out of this, the principle of *efferent interception* provides a therapeutic approach that has already proven of great value in a number of fields, while it may be said to have brought hay fever and vasomotor rhinitis definitely under medical control.

## Pioneer Medicine—Dr. Joseph O'Dwyer and Dr. Wm. Dunlop\*

By J W CRANE, *University of Western Ontario Medical School,  
London, Ontario*

ONE of the fascinations in studying pioneer life is the discovery in unexpected places of some reminder of the doctor who had in his day contributed abundantly to the health and happiness of his community. The chicken coop may be a storehouse for such finds (Fig 1). A pair of saddle bags brought to Ontario from the New England States by a United Empire Loyalist doctor was found covered with hay in the manger of an unused barn.

The University of Western Ontario was most fortunate in securing Dr. Joseph O'Dwyer's surgical bag containing several types of intubation tubes, some gold-plated, others of hard rubber, a mouth gag covered in part with chamois for protection of the gums of infants, ice cap, a partially used tube of lubricant and a reel of silk thread (Fig 2, Fig 3). These treasures were rescued when one of his relatives living near London was making her annual domestic disturbance—popularly known as spring housecleaning. The attic at such times always furnishes fuel for the fire

O'Dwyer, who began the study of medicine in London, Canada, can hardly be called a pioneer physician, except in the sense that he was a pioneer in devising an efficient intubation tube. Like other benefactors of mankind he was ridiculed, and suffered severely because of his sensitive nature. When he described his invention at a meeting of the New York Academy of Medicine, he was told he was either a knave or a fool. Poor O'Dwyer went home to bed, and stayed there for three days, not wishing to see anybody.

The more time one devotes to the study of the lives of the doctors who were "guide, philosopher and friend" to the pioneers of this country, the more one is convinced that their lives were characterized by sturdy heroism and self-sacrifice in doing the routine of their everyday life. There have been countless Dr. Macdougalls among them. The vast majority have gone to their graves "unknown, unknelt and unsung." Admiration for such noble men arouses a hope that some permanent recognition be given them. A small museum in every county could be made the storehouse for the instruments, prescription books, diplomas, professional correspondence, and other

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\*Read before the American College of Physicians, Annual Clinical Week, April 12, 1929, Boston.



This brass plate was recovered from the door, when, after the house was torn down, was used as a door to a chicken coop.

FIG 1



DR JOSEPH O'DWYER

FIG 2

FIG 1 Surgeons in England receive at graduation the degree of Bachelor or Master of Surgery and are addressed as Mr. A physician receives an M.D. degree and is known as Doctor.

FIG 2 Dr. O'Dwyer spent one year in the office of Dr. Anderson, London, Ont., later going to New York.

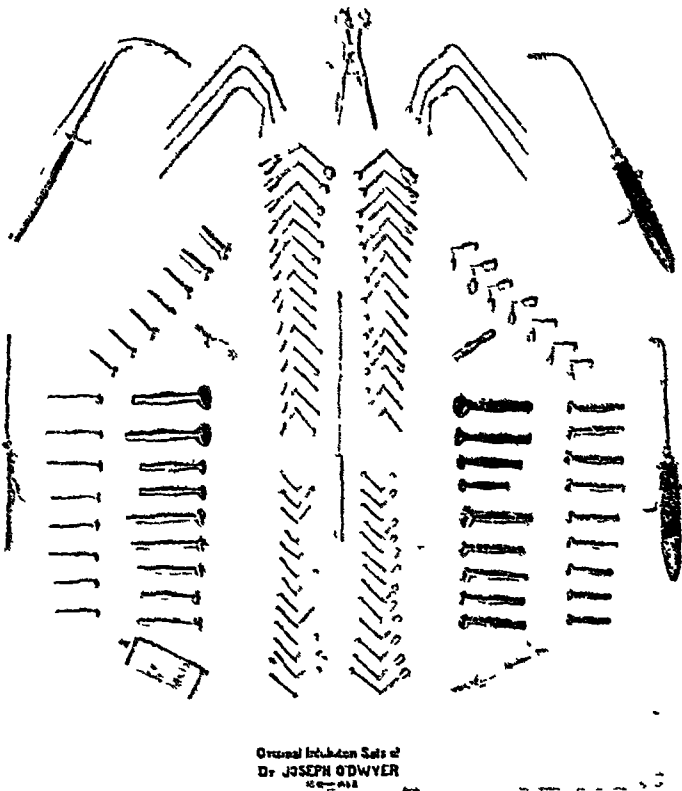


FIG 3 O'Dwyer's intubation of various sizes, his reel of silk partially used tube of lubricant, mouth gag with jaws covered with chamois, intubator and extubator.

interesting objects associated with the physicians of that community. Such material will be invaluable when the history of medicine on this continent is written, and unless an immediate effort is made to collect and preserve such mementos, the future historian will be woefully handicapped.

#### DR W DUNLOP (1792-1848)

Last century, Dr William Dunlop, a Scotchman, was one of the outstanding figures in the settlement of Western Ontario, especially that part known as the Huron Tract—the district lying between Toronto and Lake Huron. Physically he was well adapted to the pioneer life, in that he was built on generous lines. He stood six feet three inches in his stockings and measured two feet eight inches across the shoulder. “The fur,” the term used by one writer in referring to his hair, “is the genuine Caledonian redness and roughness, and the hide from long exposure to Eurus and Boreas has acquired such a firmness of texture that he shaves with a brickbat.” He was popularly known as “Tiger Dunlop,” because, while in India, he had cleared two or three islands in the Ganges of man-eating tigers. He received his education, literary, medical and convivial, in Glasgow. The illustration (Fig 4) shows a few of the twelve decanters, which he kept filled with different brands of alcoholic stimulants and which were named after the twelve apostles. His convivial propensities are reflected also in his last will and testament, a copy of which will be referred to later.

He was the author of a small octavo entitled “Recollections of the Ameri-

can War” in which he gives a breezy and vivid description of the American War. In July, 1814, he was sent to



Dr. W. Dunlop, 1792 - 1848  
"Tiger" "12 Apostles"

FIG 4 Dr Dunlop, (1798-1848) or "Tiger" Dunlop. He named the twelve decanters after the twelve apostles.

Butler's Barracks, at Niagara, and arrived the day following the engagement at Lundy's Lane.

"Waggon after waggon arrived," he tells us, "and before midday I found myself in charge of 220 wounded, with no one to assist me but my hospital sergeant who, luckily for me, was a man of sound sense and experience. The charge was too much for us and many a poor fellow had to submit to an amputation whose limb might have been preserved had there been only time to take reasonable care of it. But under the circumstances it was necessary to convert a troublesome wound into a simple one, or to lose the patient's life from want of time to pay him proper attention. I never underwent such fatigue as I did for the

first week at Butler's Barracks. The weather was intensely hot, the flies were in myriads and lighting on the wounds deposited their eggs, so that maggots were bred in a few hours,\* so that, long before I could go round dressing the patients it was necessary to begin again. For two days and two nights I never sat down. On the morning of the third day I fell asleep on my feet."

Although as a surgeon he was supposed to be a non-combatant, still he was often found in the firing line. One incident illustrates the kindness and courage of Dunlop, who at this time was only 22 years of age. He carried several of the wounded to safety, but one of them was a corpse when he reached the hospital quarters, having received a second bullet in transit.

There was urgent need during the following winter for supplies for the garrison at Mackinaw in case of siege, necessitating the building of a road from Lake Simcoe to Penetanguishene, a distance of 30 miles. Dunlop agreed to engineer the construction of this road through a dense forest with snow four to six feet deep. Bridges had to be thrown across streams, requiring men to stand in ice-cold water up to the middle. Oxen were the only method of transport. Against such odds he was able to accomplish what was regarded as the impossible, and completed the work in an incredibly short time, but much to his chagrin,

peace was declared just as the road was finished.

One night while building this road, he lost the trail in the bush and had to sleep out all night with the temperature below zero. Knowing too well the action of alcohol when taken internally under such circumstances, he poured the rum into his boots instead of into his stomach. He made a hole in a snow bank, crawled in, placed his little dog on top of him, and went to sleep. In the morning the dog was dead, his toes frozen and his hands numb, but he was able to make his way to the camp. He recovered completely in three weeks under the care of a French-Canadian who "enveloped his feet in a poultice of boiled beech leaves." Dunlop thought at that time that this was the only instance of a white man sleeping out in a Canadian winter night, without fire or covering of any kind.

At the close of the American War, his regiment was ordered to England, arriving too late to participate in the Battle of Waterloo. Dunlop, however, followed his regiment to India. He developed jungle fever and was invalided to England. His restless activity found an outlet in editing newspapers, writing articles for Blackwood's, founding a club with the euphonious name of "The Whistle and the Pig," floating industrial companies, and finally as Lecturer in Medical Jurisprudence at the University of Edinburgh. His lectures are referred to as a mixture of fun and learning, law and science blended with rough jokes and anecdotes not at all of the most prudish nature. He edited an edition of Beck's Medical Jurispru-

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\*Dr W. S. Baer of Baltimore has recently reported the successful treatment of cases of chronic osteomyelitis by applying living maggots to the wound.



dence, a book that is highly entertaining as well as instructive

As a result of a love affair, Dunlop left for Canada, having accepted the position of Warden of the Forest for the Canada Company. In 1826 he arrived in Goderich on Lake Huron and made this place his headquarters for the next eighteen years. He was joined later by his brother, Captain Robert Dunlop, of the Royal Navy, and they had as their housekeeper, Lou McColl—a very efficient and resourceful woman. Dr. Dunlop threw all his energy in securing settlers for this part of Ontario. His book, "Statistical Studies of Upper Canada," published in 1833, is filled with enthusiasm and optimism and, undoubtedly, influenced many immigrants to locate in his district. In 1841 he was elected a mem-

ber of Parliament, and continued to represent the Huron District until 1846, when he accepted a government position on the Lachine Canal near Montreal. He died in 1848 at Lake Louise, near Montreal, and faithful Lou brought his body to Goderich for burial. He asked her "to put his back up against that of his brother, in order to keep him warm." A cairn has been erected over the graves of these two remarkable pioneers on the Maitland River overlooking Goderich (Fig 5).

Records are available regarding his professional work, but these are not as appealing as those dealing with his social and convivial activities. His method of liquifying the debt owed by the brothers to their housekeeper Lou is not original but is characteristic of his initiative in solving difficult

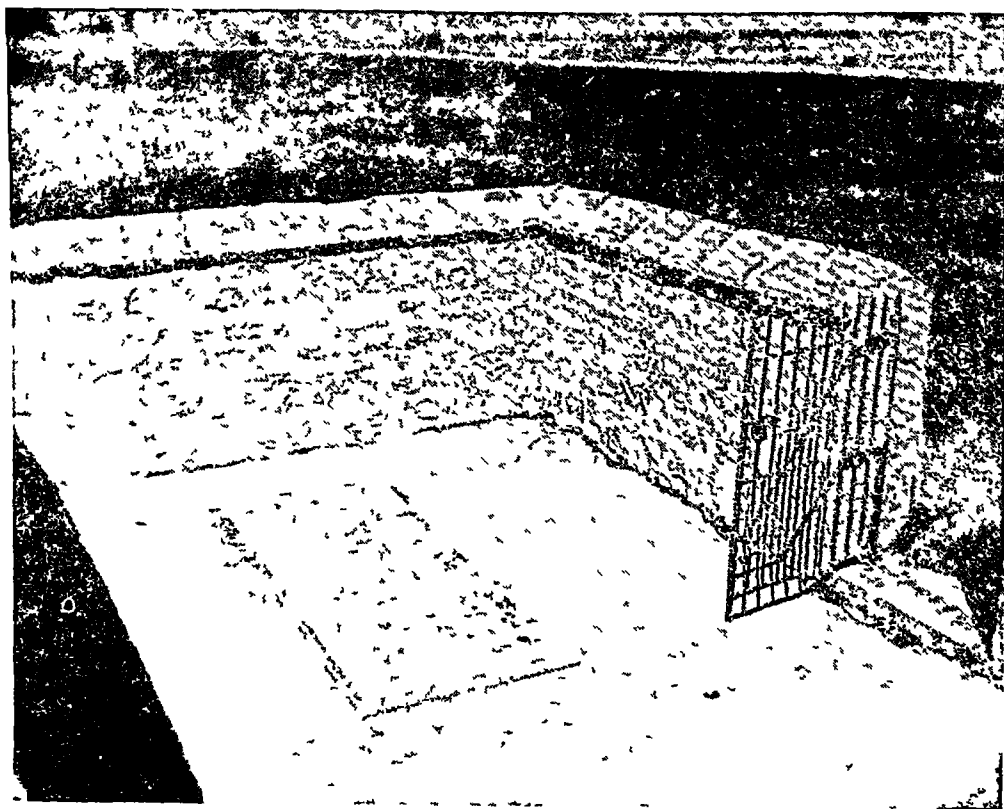


FIG 5 Cairn of Dr. Dunlop on the Maitland River overlooking Goderich

problems. The brothers held a council of war, and it was agreed that matrimony was the logical solution,—but who was to marry Lou? To settle the question the doctor suggested that it be left to a flip of a coin. He happened to have a double-headed penny, with the result that the Captain won the toss and a wife. Lou was consulted, and proved quite agreeable to the settlement. She and the Captain were married, although it has been said that Lou had a stronger attachment to “the dear doctor” than to her own husband.

#### DUNLOP'S WILL

Dr Dunlop's will is a classic in Canadian forensic history. It reads as follows:

“In the name of God. Amen. I, William Dunlop, of Gairbraid, in the township of Colborne, County and District of Huron, Western Canada, Esquire, being in sound health of body, and my mind just as usual, which my friends who flatter me say is no great shakes at the best of time, do make this my last will and testament as follows—revoking, of course, all former wills.

“I leave the property of Gairbraid and all other landed property I may die possessed of, to my sisters, Ellen Boyle Story, and Elizabeth Boyle Dunlop, the former because she is married to a minister whom (God help him!) she henpecks the latter, because she is married to nobody, nor is she likely to be, for she is an old maid and not market-rife, and also I leave to them and their heirs my share of the stock and implements on the farm, provided always that the enclosure

round my brother's grave be reserved, and if either should die without issue then the other to inherit the whole.

“I leave to my sister-in-law, Louisa Dunlop, all my share of the household furniture and such traps with the exceptions hereinafter mentioned.

“I leave my silver tankard to the oldest son of old John, as the representative of the family, I would have left it to old John himself, but he would melt it down to make temperance medals, and that would be a sacrilege—however, I leave my big horn snuff-box to him, he can only temperance horn-spoons of that.

“I leave my sister Jenny my Bible, the property formerly of my great-great-grandmother, Bethia Hamilton, of Woodhall, and when she knows as much of the spirit of it as she does of the letter, she will be another guise-Christian than she is.

“I also leave my late brother's watch to my brother Sandy, exhorting him at the same time to give up wiggery, radicalism, and all other sins that do most easily beset him.

“I leave my brother Alan, my big silver snuff-box, as I am informed he is rather a decent Christian, with a swag belly and a jolly face.

“I leave Parson Chevasse (Maggie's husband) the snuff-box I got from the Sarnia Militia, as a small token of my gratitude for the service he has done the family in taking a sister that no man of taste would have taken.

“I leave John Caddle a silver teapot, to the end that he may drink tea therefrom to comfort him under the affliction of a slatternly wife.

“I give my silver cup with a sovereign in it to my sister, Janet Graham.

Dunlop, because she is an old maid and pious, and therefore will necessarily take to horning, and also my gramma's snuffmull, as it looks decent to see an old woman taking snuff "

This short sketch of Dr Dunlop is evidence that the lives of the early physicians can fulfill the requirements needed to make this form of historical research a hobby of the practicing physician. Let him secure as a beginning the details of the medical history

of his own community. He will then see the necessity of placing in a fire-proof building such material as surgical instruments, saddle bags, diplomas and professional correspondence. If such is not feasible, it might be well to resurrect the Egyptian form of burial. Let us bury with our dead everything that may be of historical value in the future. Graves then will be as much sought after as that of King Tut.

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## Editorials

### *HOW THE SCARLET FEVER EPIDEMIC AT BERE A COLLEGE WAS CONTROLLED\**

Nothing can more strikingly illustrate the fact of the great advance in our knowledge of scarlet fever than the story of the successful management of the important epidemic of this disease occurring at Berea College, last spring. The story of the control program carried out there, based upon the newer knowledge of scarlet fever, its etiology and prevention, is of such significance in the practice of medicine, that it is considered to be well worth while to tell it again here, in the hope that it may reach some of those practitioners who might otherwise miss the local reports of the Berea epidemic. Berea College is located in Berea, Kentucky, an agricultural community with a population of about 1,600. The college students, faculty and workers number about 2,200. Most of the workers, part of the faculty and about 100 students live off of the campus. The others live in various campus dormitories. The students are largely drawn from the mountain sections of Kentucky and the surrounding states.

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\*A Practical Demonstration in the Control of Scarlet Fever. By J. L. Jones, M.D., State Epidemiologist, Louisville, and John W. Armstrong, M.D., Physician and Health Officer, Berea College, Berea (Kentucky Medical Journal, November, 1929)

Two large boarding halls, each with its own kitchen and several dining rooms, are maintained for students. The school has an independent water supply, provided through an impounding reservoir. The milk supply is largely from the college herd, and up to the time of the epidemic was being used raw. A small amount of raw milk obtained from the outside is pasteurized at the college. The college hospital, with its isolation annex for communicable diseases, cares for sick students. Medical service is provided by a staff of three physicians. During February and the early part of March, there were 12 students with scarlet fever admitted to the college hospital. All of these patients had a characteristic scarlatinal rash followed by desquamation. Later on it became apparent, on questioning the student body, that there were many mild, unrecognized cases of sore throat, associated in a majority of instances with headache, and either nausea or vomiting, or both. A few of these students had reported at the out-patient clinic for treatment, but in the absence of a recognizable rash at the time they were seen, the condition was thought to be tonsillitis. On March 11 one case only of scarlet fever was admitted to the college hospital, but on March 12, there were 94 admissions, each case having sore throat, headache, malaise and some

degree of fever. All throats had a similar appearance, scarlet arch of fauces and an exudate over the tonsils. The State Board of Health was at once notified, and its representatives in connection with the College Medical Staff immediately began an investigation. On March 13, 80 more similar cases were admitted to the hospital, and during the next three days 147 additional cases came in, after which there was a sudden drop to an average of 4 cases a day for the week following. In view of such a mass infection, it seemed at first that the epidemic was milk borne and one of septic sore throat, and control measures were at once instituted on this basis. Pasteurization of all milk was ordered, cows and milk were examined, and nose and throat cultures taken on all food handlers and dairy workers. Several carriers of hemolytic streptococci were found among students working in the boarding halls. On the second day of the epidemic, March 13, rashes began to appear. In several cases scarlet fever antitoxin was injected intradermally at the site of the rash, and typical blanching occurred, showing the condition to be scarlet fever. Hemolytic streptococci were found in cultures made from the throats of some of the patients. In all probability all cases up to March 12, when the explosive outbreak occurred, were contact infections. The sudden appearance of 94 cases on March 12, with 80, 58, 60 and 29 the following days respectively, and then the sudden drop to 4 cases per day, strongly suggested the occurrence of a milk borne infection superimposed upon contact in-

fection. This seemed more evident when it was learned that all of the cases which developed between March 12 and 16 had been eating at the same boarding hall. A probable clew to the source of infection was indicated upon finding several waiters in the hall to be carriers of hemolytic streptococci. Confronted then with a wide-spread outbreak of scarlet fever, the problem presented itself as to how it could be most effectively controlled. The services of Dr. Gladys H. Dick, of Chicago, were secured, who came to Berea, and gave advice and assistance in carrying out a modern, scientific program in the control of scarlet fever. It was decided not to close the school, or to discontinue classes. After due consideration of all aspects of the problem, the following general program of control was decided upon —

- 1 Isolation of all cases, either in the college hospital or in dormitories set aside for that purpose.

- 2 Campus quarantine of all persons connected with the college, based on the results of nose and throat cultures taken on blood agar plates.

- 3 Skin tests (Dick Test) on all persons connected with the college to detect susceptibles to scarlet fever.

- 4 Active immunization of all susceptibles with 5 graduated doses of scarlet fever toxin.

Skin tests were done, and nose and throat cultures taken on the entire population of Berea College, both procedures being carried out at the same time. Nose and throat cultures were made on 2,232 persons, 834, or 37.4 per cent of whom were positive. However, of the 834, 350 were in the

hospital with scarlet fever. Leaving this group out of consideration, there remained 1,882 on whom cultures were taken, 484 or 25.7 per cent being positive. It was known that a certain indefinite percentage of these 484 individuals had recently had mildly unrecognized cases of scarlet fever, which made it impossible to say what percentage of this group was immune carriers who had not recently had scarlet fever, and what percentage was convalescent carriers. Very few positive cultures were obtained from the nose, and all persons with positive nose cultures also had positive throat cultures. The largest percentage of positive cultures was among the student group, with the nurses coming second and the training school third. Of the 834 positive cultures which included the 350 hospital cases, 647 or 76.5 per cent were read as 4 plus, indicating that in a large majority of the individuals with positive cultures, the throat contamination was heavy. Practically all of the 350 cases of scarlet fever were in the 4 plus group. Nine and a half per cent of the positive cultures were read as 3 plus, a little over five per cent as 2 plus, and eight and nine-tenths per cent as 1 plus. Of the 834 positive cultures, 702 or 84.2 per cent were in persons with negative skin tests. However, included in the 702 are the 350 hospital cases, all of whom had negative skin tests. There were 132 persons with positive cultures who had positive skin tests. This seems rather surprising, as indicating that this number of susceptible persons had scarlet fever streptococci in their throats. According to the Dicks, however, whether a

person with scarlet fever streptococci in the throat develops scarlet fever or not depends on whether or not the dosage present is sufficient to overcome the immunity present. Complete immunity may, however, result from several attacks of mild sore throat due to the presence of these organisms. As to the relation between cultures and skin tests, of the 702 with negative skin tests and positive cultures, 548, or 78 per cent, had 4 plus culture readings, but this included all of the 50 hospital cases. Of the 132 with positive skin tests and positive cultures, 99, or 75 per cent had 4 plus culture readings, while over 11 per cent had 3 plus plates, indicating heavy contamination of the throat in a large number of susceptible persons. It was finally decided to keep all cases of scarlet fever isolated in the hospital or dormitories, and to quarantine all carriers to the college campus, release from such quarantine or isolation being based on obtaining one negative nose and throat culture. Cultures were taken once a week. In some instances, the cultures from carriers became negative in one week, the majority clearing in three weeks. In practically all carriers failing to clear in four or five weeks, pathology was found either in the nose, throat or sinuses. Among the hospitalized cases of scarlet fever, very few cultures became negative in less than four weeks, while some remained positive for five or six weeks. These findings justify the 28 day quarantine for cases of scarlet fever. Nothing in the way of treatment was found efficacious in curing the carrier condition. Fresh air and

sunshine seemed to be most helpful. After the fifth immunizing dose of toxin had been given to the susceptible group, the quarantine was raised. Of the 414 cases of scarlet fever at Berea, 139 were so mild that they were sick, clinically, for only a day or two, with temperature under 100. In 275 the temperature ranged from 100-104 for 2-5 days. A rash was recognized on 83 or a little over 20 per cent. Five others desquamated, showing rash had been present but not recognized. 56 cases were reported as having albumin in the urine. Several developed nephritis. Only 24 cases had frank emesis, although a large percentage complained of nausea. As to complications, 30 had severe cervical adenitis, 10 middle ear complications, 2 mastoiditis requiring operation, 10 peritonsillar abscess, 8 arthritis, and 7 abdominal complications, 3 requiring appendectomy. Only four of the more severe cases with complications had specific treatment, two were given scarlet fever antitoxin and two convalescent serum. All four made rapid recovery. Experience in this epidemic showed the Dick test to be a definite and reliable clinical test to determine immunity and susceptibility. While 63 cases of scarlet fever developed in persons with positive skin tests before immunization was completed, no cases occurred in persons with negative tests. Furthermore, all individuals who were convalescing from scarlet fever had negative skin tests. Of the 2,308 persons tested, 502 or 21.7 per cent were positive. The mild sore throats in this epidemic conferred immunity as well as the typical cases

of scarlet fever with rash, as shown by skin tests. Active immunization of all susceptibles brought this epidemic under complete control within 7 days, or the time necessary for giving two doses of toxin. Among the 502 susceptibles only 63 developed scarlet fever subsequent to skin testing and culturing. Of these 59 developed before the second dose of toxin had been given, and the remaining four before the administration of the third dose. Of the 63, fifty-four had positive cultures at the time of skin testing. The administration of the 5 dose series of scarlet fever toxin conferred complete immunity in 97.1 per cent of the susceptible persons as indicated by a negative skin reaction to one skin test dose, with 88 per cent negative to two skin test doses, with 88 per cent negative R doses. The failure of a certain small percentage to become completely immunized after the 5 dose series of toxin is explained on the same basis as the failure of the disease itself to confer complete immunity in a small percentage of individuals, viz., a deficient immunity mechanism. Two cases immunized with the three dose series of toxin, one, two, and the other three years previously still showed complete immunity. While practically all of the persons immunized had more or less local reaction following each injection of toxin, a majority had no other disturbances. The most severe general reactions consisted of general malaise, nausea and vomiting of short duration, and various degrees of joint stiffness, all recovering with no noticeable ill after effects. The results

reported in this study of the Berea epidemic show that such an epidemic can be adequately controlled by the following means. Nose and throat cultures on blood agar plates to detect infected individuals and carriers, with isolation and quarantine, and release from same, based on the results of such cultures. Skin tests to detect susceptible individuals. Active immunization of all susceptibles with the 5 graduated doses of scarlet fever toxin recommended by the Scarlet Fever Committee. Retests, two weeks after the fifth immunizing dose, with the administration of a sixth dose to those who still react positive to the skin test. In the light of these findings it is unnecessary today for anyone to have scarlet fever. The management of this epidemic must be regarded in the light of a great confirmation and justification of the splendid work of the Dicks.



## Abstracts

*The So-Called Hyperglycemic Action of Insulin* By I Neuwirth, F Co Tu and G B Wallace (Proc Assoc of Exper Biol and Med, December, 1929, p 194)

Collens and Murlin have recently reported that the portal injection of insulin into dogs, in dosage of 0.05 to 0.1 unit per kilo weight, results in an immediate sharp rise of blood sugar of 20 to 80 mg. The rise occurs within 5 minutes and is then followed by a rapid decline. No such rise occurs following the systemic injection of the same dose of insulin. About the same time Bürger and Kramer reported that the injection of 10-20 units of insulin into the cubital vein of human beings produces a rise of blood sugar averaging 11.5%, intrajugular injection of 40 units into dogs of about 20 kilograms causes a rise averaging 28%, intraportal injection results in a rise averaging 46%. The rises occur within 5 minutes and are followed in 10-30 minutes by a rapid fall. In both of these reports the results are interpreted as showing that insulin has a glycogenolytic action of the liver and that the hyperglycemia is a physiological or normal response to this action. The present investigators carried out experiments on dogs corresponding to those described in the reports cited. They used the Lilly insulin, as did Collens and Murlin, whereas the Burroughs Wellcome product was used by Bürger and Kramer. Using small doses, they obtained no rise in blood sugar on intrajugular injection, but a rise followed intraportal injection. Their maximum rise was 15 mg as compared to the 20-80 mg rise of Collens and Murlin. With the larger dosage, 2-3 units per kilo (40 units total) they obtained a rise on intrajugular injection of 5 to 10%, and on intraportal injection of 15%, as compared to the 28% and 46% averages of Burger and Kramer. Their results, however, were confirmatory

of the occurrence of a rise. Repeating their experiments with crystalline insulin prepared at the Johns Hopkins laboratory, in corresponding dosages, they found the injection intrajugularly or intraportally to cause a fall of blood sugar within 1-10 minutes with no rise at 3-6 minute intervals after the injection. Since the only difference here is in the form in which the insulin is administered, it appears that the hyperglycemia when obtained, is not a true insulin action, but is due to some substance in the commercial product which acts on the liver. Fisher's experiments in which he showed that there could be obtained from the pancreas and other tissues, a toxic substance which among other actions, caused a rise in blood sugar, become of interest in this connection.

*The Treatment of Lobar Pneumonia with Concentrated Antipneumococcus Serum* By Russell L Cecil and W D Sutliff (Jour of A M A, December 29, 1928, pp 2035)

For two years these authors carried out studies on the specific treatment of lobar pneumonia at Bellevue Hospital, largely confined to investigation of the immunologic properties and the therapeutic value of concentrated antipneumococcus serum prepared according to the method of Felton. The summary of this work appears to indicate the following. Refined antipneumococcus serum is a purified and concentrated derivative of ordinary antipneumococcus horse serum. It is usually prepared in a polyvalent form, containing immune bodies against pneumococcus types I, II and III. Its potency against type I and type II is quite high. Its potency against type III is insignificant. Concentrated serum, when injected intravenously into monkeys infected with lethal doses of pneumococcus type, promptly sterilizes the blood and

causes a rapid resolution of the pneumonic exudate. When concentrated serum is injected intravenously into patients in the early stages of pneumococcus type I pneumonia, a striking clinical effect is usually obtained. The bacteria disappear from the blood and the temperature falls to normal. Even in late cases, good results are often obtained. In type II pneumonia the clinical results are not so impressive, though here again in patients treated early, favorable results are often noted. In type III pneumonia, no clinical effect has been observed. In type IV pneumonia the beneficial effect of serum is questionable. In 441 cases of lobar pneumonia treated with refined polyvalent serum, the death rate was 30 per cent. In a control series of 444 cases the death rate was 39.2 per cent. In respect to the death rate, the refined serum produced its most striking effect in pneumococcus type I pneumonia. In a series of 153 cases of type I treated with the serum the death rate was 20.9 per cent, while a control series of 147 untreated type I cases showed a death rate of 32.6 per cent. A definite but less marked effect on the death rate was observed in cases of pneumococcus type II pneumonia treated with concentrated serum. The serum had no effect on the death rate in the pneumococcus type III pneumonia. In type IV pneumonia the death rate was lower in the treated than in the untreated series, but factors other than serum may have been responsible for this difference.

*The Control of Scarlet Fever* By George F. Dick and Gladys H. Dick (Amer Jour of Dis of Children, November, 1929, p. 905)

Six years ago these investigators began the publication of a series of experiments which established a specific type of hemolytic streptococcus as the cause of scarlet fever. In these experiments it was shown that the scarlet fever streptococcus produces a potent soluble toxin which is responsible for the toxemia, nausea and rash, and that recovery from the disease with subsequent immunity depends on the production of an antitoxin. The conclusions as to the etiology, specific toxin and anti-

toxin of scarlet fever have been verified by numerous reports in this and other countries, particularly that done by Nicolle in the Pasteur Institute in Tunis, where all the crucial experiments were repeated, including even the production of experimental scarlet fever in human beings. Results are now available from observations made during the last six years on a series of 32,440 persons on whom skin tests were made, on 11,584 susceptible persons who were immunized against scarlet fever by the injection of graduated doses of the sterile toxin, and on groups of susceptible persons found to be infected after exposure who were given prophylactic doses of the antitoxin. All these persons were exposed to scarlet fever in one or more epidemics. Results are also available from observations in a series of 967 cases of scarlet fever in which the antitoxin was employed therapeutically. The reliability of the skin test in determining susceptibility to scarlet fever is shown by the results in 20,856 persons with spontaneously negative reactions. All of these immune persons passed through one epidemic of scarlet fever, and some went through several epidemics without contracting the disease, with the possible exception of one boy who showed a desquamation of the feet and gave a history of sore throat. The most severe test of the skin reaction was found in a group of 2,157 pupil nurses and interns who were allowed to go duty in contagious disease services when their skin tests were found to be spontaneously negative. In spite of prolonged and intimate exposure to scarlet fever, none of this group contracted the disease. Regarding the incidence of immunity to scarlet fever after early infancy this depends on conditions that favor exposure to the disease. Thus in an overcrowded institution the incidence of susceptibility may be as low as 10 per cent, while in rural or suburban groups it may be as high as 85 per cent. In a series of skin tests, it will be found that the positive reactions show all gradations from small areas of faint color to intensely red reactions 3 to 5 cm in diameter. These differences in the intensity of the skin reactions correspond to differences in

degree of susceptibility, and partly explain the great variation in severity of scarlet fever. The intermediate stages of the reaction also indicate that in many persons immunity to scarlet fever is acquired gradually through repeated infections with the streptococci of scarlet fever without the development of a typical attack of the disease. It has been learned that one attack of scarlet fever sore throat does not necessarily confer complete immunity, but typical attacks of scarlet fever usually result in complete immunity, as indicated by negative skin reactions in patients convalescent from scarlet fever and by the comparative infrequency of second attacks. Active immunization with graduated doses of sterile scarlet fever in 12,785 susceptible persons caused no injury in any instance. In three institutions urine analyses were made before, during and after immunization, and there was no evidence of nephritis caused by the immunization. Some persons who had nephritis were immunized without causing an exacerbation of the condition. In a large series, including highly susceptible persons, general reactions may be expected after each dose in about 10 per cent. The most highly susceptible persons usually react more strongly on the first doses, others may not have any reactions until the fourth or fifth dose is given. As a rule, reactions after the last and largest dose are fewer and milder than after the smaller first doses. The immunizing doses should be accurately graduated, and it is important to give them in the proper sequence in order to avoid unnecessarily severe reactions. Experimentally, as much as 20 cc of undiluted toxin containing nearly 1,000,000 skin test doses have been injected without causing injury and without producing nephritis in human beings. Strong warning is given against the use of the Larson ricin treated toxin, in spite of repeated warnings it has been widely distributed and employed by physician in unsuccessful attempt to control epidemics of scarlet fever. The doses of sterile toxin for active immunization should be graduated, beginning with 500 skin test doses in the first injection and increasing to 80,000

or 100,000 skin test doses in the last. The injections are made subcutaneously at intervals of one week. If the full amount is given in each dose, the five doses may be counted on to immunize completely 95 per cent of susceptible persons, and to modify considerably the susceptibility of the rest. Two weeks after the last dose is given another skin test is made, using 0.1 cc of the skin test solution or one skin test dose on the right arm, and 0.2 cc, or two skin test doses on the left arm. If the reaction on either arm is positive, the fifth dose is repeated. Unless the immunization is carried to the point of a negative skin reaction, complete protection against scarlet fever cannot be expected, although the severity of a subsequent attack would be modified by the partial immunization. The duration of active immunity, as well as the degree of immunity, depends on the amount of toxin injected. Retests made at intervals of 1, 2 and 3 years indicate that more than 90 per cent of these immunized to the point of an entirely negative skin reaction retain their immunity. Between 5 and 9 per cent slip back and require a second immunization. By means of nose and throat cultures on blood agar plates, skin tests for susceptibility, active immunization of susceptible persons with the toxin and the use of antitoxin prophylactically in infected susceptibles, it is possible, in a group small enough to test and culture in one day, to bring an epidemic of scarlet fever under control in forty-eight hours. The passive protection conferred by a prophylactic dose of any antitoxin is transient, lasting at the most from two to three weeks. Active immunization with the toxin should be begun in the infected susceptibles one week after the prophylactic dose of antitoxin is given. Scarlet fever antitoxin may be employed therapeutically with advantage in all cases of scarlet fever as soon as the appearance of the rash suggests the diagnosis. Given early, in adequate dosage, scarlet fever antitoxin gives brilliant results. The patient sometimes recovers so quickly that the attending physician wonders whether or not he could have been mistaken in his diagnosis of scarlet fever.

The longer the patient goes without antitoxin, the less he benefits from it when given. It should not be withheld until it becomes apparent that the attack is a severe one, but should be given in time to prevent the development of a severe attack. Reports as to the effect of scarlet fever antitoxin in reducing the complications are sometimes conflicting, due to delay in administering the serum in some cases, or to the use of poor preparations of antitoxin. Most scarlet fever antitoxins of European manufacture are considerably weaker than the best American serum. Samples of antitoxin purchased in Europe have been found to contain from a trace to 5,000 neutralizing units per cubic centimeter, while the best supplied in America contains 30,000 units. Even with the delay involved in the diagnosis of scarlet fever in hospital cases, it has been shown that scarlet fever antitoxin reduces the incidence and severity of complications. Results in the antitoxin series, which included the more severe cases, compared with the results in the control series, comprised of the cases which, on admission to the hospitals, appeared to be less severe, show that mastoiditis occurred three times as frequently in the control series as in the antitoxin series, that post scarlatinal nephritis appeared four times as frequently in the control series as in the antitoxin series, and that in spite of the milder appearance of the disease at the onset, the death rate in the control series was twice that in the antitoxin series.

*Bacteriology of the Blood and Joints in Rheumatic Fever.* By Russell L. Cecil, Edith E. Nicholls and Wendell J. Stainsby (Jour of Exper Med, November, 1929, p 617)

During the Spring of 1928, 29 patients with acute rheumatic fever were subjected to blood cultures, of whom 9, or 31 per cent, yielded a streptococcus. The higher percentage of positive cultures in the 1929 series appears to have been due to improved cultural methods. Of the 35 strains of streptococci recovered from blood cultures, 33 have been classified as alpha streptococci (*Str viridans*), one as a beta streptococcus (*Str hemolyticus*), and a gamma streptococcus (*Str anhemolyticus*). Some of the *viridans* strains produced very little green on blood media. Agglutination and absorption tests indicate that the strains of streptococcus *viridans* recovered from the blood of patients with rheumatic fever show a tendency to fall into specific biological groups. In 7 patients with rheumatic fever who were subjected to cultures from affected joints, 5, or 71.4 per cent, yielded a streptococcus *viridans*. In 3 patients in whom green streptococci were recovered from both the blood and joint, agglutination and absorption tests proved the identity of the strains isolated from the two sources. These findings corroborate those of previous investigators and make it difficult to escape the conclusion that rheumatic fever is a streptococcal infection usually of the *alpha* or *viridans* type. The pathogenesis of rheumatic fever in respect to the joint lesions appears to be analogous to that of infectious arthritis and gonococcal arthritis. Bacterial allergy probably influences the clinical picture in all three conditions, but in each instance the joint manifestations are primarily dependent upon localization of bacteria in the joint, with subsequent infection.

## Reviews

*Bacteriology for Nurses* By HARRY W CARRY, A B, M D, Assistant Bacteriologist, Bender Hygienic Laboratory, Albany, N Y, Pathologist to the Samaritan Hospital, Trop, N Y, Cohoes Hospital, Cohoes, N Y, and Putnam Memorial Hospital, Bennington, Vermont Third Revised and Enlarged Edition Illustrated with 43 engravings and 1 colored plate, 282 pages, F A Davis Company, Philadelphia, 930 Price in cloth, \$2.25

The second edition of this book appeared ten years ago, and since that time much advance has been made in bacteriology. In order to incorporate this new work, it has been necessary to rewrite the entire book and to enlarge it. Many of the subjects have been discussed in more detail than might seem to be required in a text-book for nurses, but the requirements of the National League for Nursing and the State Board of Education are more exacting than they were formerly. The author has had it in mind to prepare a book to serve the nurse, not only as a text-book, but for reference as well. This book appears to cover the ground of general bacteriology sufficiently thoroughly for the purpose for which it is intended. A series of fifteen laboratory exercises is given, and these afford practical application of the material given in the text. The book is written in clear and simple language, and the exposition is also clearly stated. It may be recommended for the purpose for which it was written, a text-book of bacteriology for the practical nurse.

*Surgical and Medical Gynecologic Technic*

By THOMAS H CHERRY, M D, F A C S, Professor of Gynecology in the New York Post-Graduate Medical School and Hospital, etc. 678 pages, 558 half-tone and line engravings, from photographs

and pen and ink drawings by the author. F A Davis Company, Philadelphia, 1929 Price in cloth, \$8.00

This book was written with the object of presenting to the medical profession a technical work on gynecology. His experience as a teacher for the past fifteen years in the New York Post-Graduate Medical School has impressed him with the needs of graduate medical students in both surgical and non-surgical procedures. The book is not intended as a textbook for the undergraduate student of medicine, as the necessary rudiments, such as physiology, symptomatology and diagnosis have largely been omitted. To the practitioner of medicine, who is constantly coming in contact with gynecological patients and to whom they look for relief, this book is intended to aid him in applying appropriate modern methods of diagnosis and therapy. To the practitioner who has had and comprehends surgical technic, with especial leaning towards gynecology this book is further intended to help him to select standard operative procedures for those patients requiring surgical intervention. The description of operations is confined to one standard method, which in his own experience has given the best result. The author has attempted to represent in this work a single method of therapy, based upon anatomy and pathology and to give sufficient illustrations to make this logical and comprehensive. The illustrations, while home-made, serve their purpose very well, and are on the whole very good. The arrangement of the material is very good, and the various technical methods are clearly presented.

*Incompatibility in Prescriptions and How to Avoid It* To Which is Added a Dictionary of Incompatibilities By THOMAS STEPHENSON, D Sc, Ph C, F R S Edin,

FCS, Editor of the Prescriber, Some Time Examiner to the Pharmaceutical Society of Great Britain, Author of the Prescriber's Pharmacopoeia New Edition, Revised and Enlarged 61 pages Paul B Hoeber, Inc, New York, 1929 Price in cloth, \$1.50

This little book originally appeared in 1915 in the form of a 32-page pamphlet. It apparently filled a want, as reprintings were called for in 1916 and again in 1921. A second edition carefully revised was issued in 1924, and reprinted in 1925. As only a few copies of this remain unsold, this new edition has been called for. Opportunity has been taken for a thorough revision of the entire work, and of adding for reference purposes a complete Dictionary of Incompatibilities. It is now possible to ascertain with a minimum of trouble the exact difficulties to be encountered in dispensing any of the drugs now in common use. The work is practically a new book, and its size has been increased to double that of the original pamphlet. As far as possible the incompatibilities described in the following pages have been verified experimentally. It is intended in these pages to study the subject of incompatibility in a systematic manner, illustrating with examples the various difficulties most likely to be met with by the physician in ordinary practice. For the latter this little volume will prove to be most serviceable and practical.

*Outline of Preventive Medicine* For Medical Practitioners and Students. Prepared Under the Auspices of The Committee on Public Health Relations of the New York Academy of Medicine. 21 Contributors. Editorial Committee: Frederic E. Sandern, Charles Gordon Heyd and E. H. L. Corwin. 389 pages. Paul B Hoeber, Inc, New York, 1929. Price in cloth, \$5.00.

Repeated requests for an outline of the practical features in the prevention of disease induced the Public Health Relations Committee of the New York Academy of Medicine to appoint a sub-committee for the purpose of assembling and supervising

the publication of a brief manual of the subject. Each contributor to this volume has written of the ways in which his specialty is related to preventive medicine, limiting his contribution to salient suggestions based on individual experience, without any attempt at textbook completeness. The list of contributors comprises Harlow Brooks, Robert A. Cooke, E. H. L. Corwin, Charles L. Dana, R. L. Dickinson, A. B. Duell, H. S. Dunning, Alice Hamilton, C. G. Heyd, R. A. Hibbs, Arnold Knapp, S. W. Lambert, G. M. MacKee, J. A. Miller, James Pedersen, Bernard Sachs, F. E. Sandern, J. B. Squier, P. Van Ingen, B. P. Watson and C. H. Watson. The various contributions making up this volume constitute a valuable resume of the practical features in disease prevention, and should be of great value to the general practitioner in preparing himself for the part he should play in furthering the cause of preventive medicine. Much valuable information is contained herein, and the volume is not so technical that it cannot be recommended for use by laymen.

*Synopsis of the Practice of Preventive Medicine* As Applied in the Basic Sciences and Clinical Instruction at the Harvard Medical School. Edited by Dr. SHIELDS WARREN. 194 pages. Harvard University Press, Cambridge, 1929.

This book has a similar aim, and covers practically the same ground as the Outline of Preventive Medicine prepared by the New York Academy of Medicine. It was not conceived as a text or reference book but merely as a depository for such points as seemed of possible value in emphasizing the importance of preventive medicine for the practitioner. The various chapters represent the composite ideas of many of the faculty, and stress those prophylactic measures that should help the doctor in protecting the health of his patients. The collection represents each department of the school in a presentation of the pertinent things relating to prevention that each department felt could and should be taught in that department. As a matter of fact it provides essentially a small, collective text-

book of general practice of preventive medicine, and is intended to further the permeation of the whole curriculum with the atmosphere of preventive medicine as equal in strength to that of curative medicine. In carrying this out, purely preventive measures have been blended with those that check or control the progress of slight or early chronic diseases. There is a very great unevenness in the various sections, those on Bacteriology, Medicine, Surgery and Pediatrics contain the most pertinent material. The two pages devoted to syphilology represent a good opportunity lost. As compared with that produced by the New York Academy of Medicine, the Harvard book has much less material and in general is less specific in its application to preventive medicine and less practical.

*Pettibone's Textbook of Physiological Chemistry* With Experiments Revised and rewritten by J. F. McCLENDON, Ph.D., Professor of Physiological Chemistry, Medical School, University of Minnesota. Fourth Edition. 368 pages, 17 illustrations. The C. V. Mosby Company, St. Louis, 1929. Price in cloth, \$3.75.

The author's aim in writing this book was to prepare an intermediate textbook which would cover the general field of physiological chemistry in such a way as to give students a familiarity with compounds important from a biochemical viewpoint and to acquaint them with the fundamental processes which go on in the animal body. He has attempted to avoid confusing the beginner with lengthy discussions of debated points, but to set forth as clearly as possible the present status of our knowledge. The material is so chosen that the book may be used for intermediate classes, or for advanced work when supplemented by lectures. The appended laboratory work has been drawn from the manual in use in his classes during the last five years. Since this first edition the following ones have preserved the original character of the work, with much new material added, both in the text and laboratory section, and some of the older methods have been

omitted. This fourth edition has been revised and rewritten, so that it has been brought up to date, and now serves as a complete textbook of physiological chemistry. The material is presented in a clear and logical manner, and with a readable style.

*An Outline of Endocrinology* By W. M. CROFTON, B.A., M.D., Lecturer on Special Pathology, University College, Dublin, Pathologist, Dr. Steevens Hospital, Dublin. Second Edition. 163 pages, 53 figures. William Wood & Co., New York, 1929. Price in cloth, \$3.00.

This book consists of the substance of lectures given annually by the author since 1910. He has had in mind the production of a short but sufficiently comprehensive textbook on the Internal Secretions, both for the medical student and the general practitioner. The reception of the first edition was so encouraging that the author has brought out this second edition, brought as far as possible up to date with the very rapidly advancing work on the endocrine mechanisms. The chapters include those on the pineal gland, pituitary gland, suprarenals, thyroid, parathyroids, thymus, gonads, gastrointestinal hormones, pancreas and liver, with epilogue, and supplementary notes on recent advances. The main points of our knowledge of endocrinology are given, somewhat superficially in some instances. Microbic infection as the cause of the fundamental derangements of the endocrine glands is too much emphasized, and the author appears somewhat over-enthusiastic also in his statements as to the successful use of glandular therapeutic preparations.

*The Eye in General Medicine* The Constitutional Factor in the Causation of Disease. With Special Reference to the Treatment of Diseases of the Eye. By A. MAITLAND RAMSAY, M.D., LL.S., Fellow of Royal Faculty Physicians and Surgeons, Glasgow, Consulting Ophthalmic Surgeon, Glasgow Royal Infirmary. Second Edition of "Diathesis and Ocular Diseases." 255 pages. Wil-

ham Wood & Co, New York, 1929  
Price in cloth, \$5.00

This little book was originally entitled "Diathesis and Ocular Diseases," when first published in 1909, and has been out of print for some years. This, the second edition, has been almost wholly rewritten, and so completely rearranged that, although the theme is the same, the book itself is new. It claims to be no more than a personal record of a fairly long clinical experience, and is published in the hope that it may be useful both in the junior practitioner and to the young ophthalmologist. Although the book is intended to be read as a whole, yet each chapter is complete in itself. This book contains a good deal of very important information with reference to some of the ocular manifestations of disordered carbohydrate metabolism, defective elimination, etiology of acute primary glaucoma, medical aspects of eye strain, pneumococcal ulceration of cornea, toxic inflammation of the iris, ocular manifestations in cardiovascular disease, etc., of which the general practitioner should have knowledge. For him this book should possess a special practical value.

*The Newer Knowledge of Nutrition* By E. V. McCOLLUM, Ph.D., Sc.D., Professor of Chemical Hygiene in the School of Hygiene and Public Health, of the Johns Hopkins University, and Nina Simmonds, Sc.D. (Hygiene), Formerly Associate Professor of Chemical Hygiene in the School of Hygiene and Public Health, of the Johns Hopkins University. 594 pages, 34 illustrations. Fourth Edition. Rewritten. The MacMillan Company, New York, 1929. Price in cloth, \$5.00.

Advances along several lines since the publication in 1925 of the third edition of this book make necessary an extensive revision in order to include the most important studies relating to several phases of nutrition. The general plan of the third edition has been preserved, and while much of the former edition has been retained, the book has been essentially rewritten for the purpose of elimination of some parts and the condensation of others, so as to make

room for the new experimental work without enlargement of the volume. The original purpose of preparing a comprehensive treatise on the science of nutrition, in which the newer knowledge is presented in its historical setting, has been adhered to. The literature has been examined to May, 1929. The bibliography of the third edition contained 1870 references. To cover the entire field of nutrition with the same thoroughness today would require the citation of about 8000 communications. Obviously it was not possible to include a complete bibliography without making the volume too unwieldy. Furthermore, the bibliography of nutrition is so easily available in Chemical Abstracts and in the Quarterly Cumulative Index Medicus, which are accessible in numerous libraries that it would hardly be justified in publishing an exhaustive list of publications on the subject. For these reasons the authors have included only a select bibliography, but have made an effort to include all papers which contain important special lists of literary citations. Among the most striking features of the new edition are the recent discoveries concerning the etiology and treatment of the anemias, both secondary and pernicious, discussion of all that is known about the dietary requirements of blood regeneration, the experience of recent years in the control of goiter through the provision of iodine, recent researches on the relation of diet to bone development, the calcification of fractures, and the prevention of rickets. The story of the discovery of ergosterol, the mother substance of vitamin D, the active principle of cod-liver oil is given. The physiologic effects of light and the changes it effects in ergosterol, the present status of light therapy through the use of sunlight and the various sources of the ultraviolet rays, and the nutritional influence of the infra-red rays are discussed in full, as is also the relation of diet to pellagra. The chapter on the dietary habits of man is of especial interest. All is told in an agreeable easy style, and the material assembled in this work makes it of first class importance to the physician.



## College News Notes

Announcement has been made recently of the retirement of George E. Vincent, Ph D, from the Presidency of the Rockefeller Foundation. Dr. Vincent was the guest speaker at the annual Banquet of the College at Boston last year. He is succeeded by Dr. Max Mason.

Dr. James H. Hutton (Associate), President-Elect of the Chicago Medical Association, addressed the Franklin County Medical Society at Eldorado, November 26, on "Endocrine Disturbances and the Common Cold."

Dr. Albert M. Snell (Fellow), Rochester, Minn., addressed the Northern Minnesota Medical Association at its last annual meeting, on "Recent Advances in Endocrinology."

Dr. W. W. Duke (Fellow), Kansas City, spoke before the St. Louis Medical Society, December 10, on "Allergy as Related to the General Practice of Medicine."

Dr. Frederick Epplen (Fellow), Seattle, spoke on internal medicine and diagnosis during the opening exercises of the new medical library of the Spokane County Medical Society during November.

Dr. Julius H. Hess (Fellow), Chicago, gave an exhibition before the U. S. Live Stock Sanitary Association, December 4-6, at Chicago on "Clinical Aspects of Human and Animal Rabies," illustrated by moving pictures.

Dr. Carl V. Weller (Fellow), Ann Arbor, Mich., was made Secretary of the American Society for Experimental Pathology at its last annual meeting.

Dr. Kenneth M. Lynch (Fellow), Professor of Pathology at the Medical College of

South Carolina, was elected President of the American Society of Tropical Medicine at its last annual meeting.

Dr. G. Morris Golden (Fellow), Professor and Head of the Department of Medicine, Hahnemann Medical College and Hospital of Philadelphia, was the chief speaker at the December meeting of the Germantown Homeopathic Medical Society in Philadelphia held on December 16. His topic with a blackboard presentation in colors of "Methods Useful to the Practitioner in Estimating the Cardiac Function."

Dr. Vernon C. Rowland (Fellow), Cleveland, Ohio, was elected President of the Academy of Medicine of Cleveland at the annual meeting of the Board of Directors recently. Dr. Rowland is Visiting Physician at St. Luke's Hospital, Associate Professor of Medicine in the Western Reserve University Dental College and Editor of the Academy Bulletin.

Dr. H. V. Paryzek (Fellow), Cleveland, Ohio, was elected Vice President of the Academy at the same meeting. Dr. Paryzek has been a Director of the Academy for several terms. He is Instructor in Medicine at Western Reserve University School of Medicine, Visiting Physician to the Cleveland City and St. Alexis' Hospitals and Director of Laboratories at St. Alexis' Hospital.

Dr. E. Roland Snader, Jr. (Fellow), Philadelphia, is author of "A Report of two Cases of Thyroid Obesity," which appeared in the November Issue of The Hahnemannian Monthly.

Dr. James L. McCartney (Fellow), Hartford, Conn., delivered a radio address entitled "Why Folks Fail" over Station WTIC, Hartford, Conn., on December 26.

Dr Henry I Klopp (Fellow), Superintendent of the Allentown, Pa., State Hospital, read the Seventeenth Annual Report of that institution at the meeting of the Homeopathic Medical Society of the State of Pennsylvania held at Philadelphia in September. This very interesting report was published in the November edition of the Hahnemannian Monthly.

Dr Bernard L. Wyatt (Fellow), Tucson, Ariz., has accepted an invitation to do the editorial work from the medico-social point of view on *Acta Rheumatologica*. At the Budapest Congress of the Ligue Internationale Contre Le Rheumatisme, it was decided to publish *Acta Rheumatologica*, the editorial staff to be recruited from all affiliated nations. The invitation was extended to Dr Wyatt through Dr J. Van Bremmen, Chief Editor and Director of the *Acta Rheumatologica*, Amsterdam, Holland.

Dr Sinclair Luton (Fellow), St. Louis, Missouri, addressed the Fayette and Clinton (Illinois) County Medical Societies at Greenville, Illinois, recently on "Common Disorders of the Heart."

At the 28th annual meeting of the Frisco System Medical Association at Tulsa, Okla., during October, Dr Luton presented "Moving Pictures of the Heart Action."

At the annual meeting of the Southern Illinois Medical Association at Benton, Ill., November 7-8, 1929, Dr Luton presented the following papers:

"Endocarditis and Valvular Disease," illustrated with slides, "Valves of the Heart in Action," illustrated by motion pictures.

Dr Carl V. Vischer (Fellow), Philadelphia, and his son, Carl V. Vischer, 3rd, ten, took part in the Cornerstone laying of the new \$1,500,000 St. Luke's Children's Homeopathic Hospital on December 11. Dr Vischer is a Visiting Physician of the institution and is the son of the Founder and first Surgeon in Chief of St. Luke's Hospital.

Dr Francis M. Pottenger (Fellow), Monrovia, Calif., has become a Life Member of the American College of Physicians,

as of January 1, 1930. This is a manner in which many Fellows of the College could contribute to the cause of Internal Medicine, for by building up a fair Endowment Fund for the College, its work can be expanded to greater fields.

Dr Kano Ikeda (Fellow), St. Paul, Minn., has accepted the directorship of the laboratories of the Charles T. Miller Hospital, St. Paul, beginning January 1, 1930. Dr Ikeda was formerly Director of Laboratories at the St. Luke's and Children's Hospitals, St. Paul.

At the 46th annual convention of the Tri-States Medical Association of Mississippi, Arkansas and Tennessee, at Memphis, January 14-16, 1930, Dr George R. Minot (Fellow), Boston, Dr W. McKim Marriott (Fellow), St. Louis, Dr Charles C. Bass (Fellow), New Orleans and Dr Henry A. Christian (Fellow), Boston, were among the guest speakers.

Dr Russell S. Boles (Fellow), Philadelphia, was recently appointed Visiting Physician to the Philadelphia General Hospital.

Armistice Night was celebrated by the Philadelphia County Medical Society at a dinner at which Surgeon Generals M. W. Ireland (Fellow), Charles E. Riggs (Fellow) and Hugh S. Cumming (Fellow) of the U. S. Army, Navy and Public Health Service, respectively, were speakers.

Dr John A. Lepak (Fellow), St. Paul, Minn., has become a Life Member of the American College of Physicians, as of January 1, 1930.

Dr W. H. Stoner (Fellow), formerly with E. R. Squibb & Sons, has recently become affiliated with Hoffman-La Roche, Inc., of Nutley, New Jersey.

The College acknowledges receipt of the following publications by Fellows of the College:

"The Individual's Responsibility and The State's Responsibility," by Dr Frederic J Farnell, Providence, R I

"Mouth Infection," by Dr Oliver T Osborne, New Haven, Conn

The publications of members are sought by the College, in order that it may have a more or less complete library of work produced by its members

Dr S Calvin Smith (Fellow), Philadelphia, has delivered the following addresses recently

"Heart Irregularities" before the Montgomery County Medical Society, Norristown, Pa, November 6,

"The Clinical Significance of the Irregular Pulse," before the Clearfield County Medical Society, Clearfield, Pa, November 22,

"The Heart in Advancing Years," before the Harrisburg Academy of Medicine, Harrisburg, Pa, on December 22

Dr Daniel N Silverman, (Fellow), was elected President of the New Orleans Gastro-Enterological Society at its annual meeting January 23, 1930

Dr John H Musser, (Fellow), was the orator of the evening and spoke on "Gastric Ulcer"

Dr Ernest H Falconer, (Fellow), San Francisco, Calif, has subscribed to the Endowment Fund of the College and becomes a Life Member, as provided in the By-Laws

Dr Benjamin Goldberg, (Fellow), Chicago, will give the Annual Address at the meeting of the Boston Tuberculosis Association on the afternoon of Monday, February 3, 1930 His subject will be "Present Needs in Tuberculosis Control" In the evening Dr Goldberg will address the Trudeau Society of Boston on "The Medical Aspects of Phrenic Surgery"

Dr Konrad Birkhang, (Fellow), gave the annual Sigma Nu address at Mount Union College, Alliance, Ohio, on January 16th, on "An Epic in Experimental Medicine The Life of Dr. Otto Obermeier" On

January 15th, he addressed the Alliance Medical Society, Alliance, Ohio, on "Bacterial Allergy in Rheumatic Fever, Tuberculosis and Syphilis"

Dr J Dwight Davis, (Fellow), formerly of the Mayo Clinic at Rochester, Minnesota, has opened offices at 802 Wilshire Medical Building, 1930 Wilshire Boulevard, Los Angeles, Calif

The Committee on Organization of the First International Congress on Mental Hygiene, acting as representatives of national mental hygiene societies and related organizations throughout the world, has announced a world meeting on medical hygiene to be held at Washington, D C, May 5-10, 1930 The Committee on Organization has asked the co-operation of all Governments, voluntary organizations and individuals interested in better mental health for all people, in making this first world Congress on Mental Hygiene of vital significance to the cause it would serve

Dr William A White, (Fellow), Washington, D C, is President of the Congress, Dr Hugh S Cumming, (Fellow), Surgeon-General of the U S Public Health Service, is a vice president, Dr Charles F Martin (Master), Montreal, is an honorary vice president

The Elliott Chair of Preventive Medicine and Public Health has recently been established at Queen's University at Kingston, Ont, by Mr Samuel Insull, of Chicago, in honor of Dr Arthur R Elliott, (Fellow), Chicago Dr Elliott is a Queen's graduate Dr John Wyllie, M A, M B, Ch B, BS, D P H, was appointed to this Chair on December 12

Dr Walter W Palmer, (Fellow), New York, was one of the speakers at the opening of the new \$2,000,000 New York State Psychiatric Institute and Hospital, a unit of the Medical Center at Broadway and 168th Street, on December 3

Dr Ray M Balyeat, (Fellow), Oklahoma City, during November, addressed the York-

ville County Medical Society, New York, on "Importance of Pollen as an Etiologic Factor in Allergic Diseases in the Southwest Compared with Other Sections of the United States"

Dr Lawrence Litchfield, (Fellow), Pittsburgh, was the recipient of a testimonial dinner in December, just previous to his departure south for the winter Dr William S Thayer, (Fellow), Baltimore, was one of the speakers

Dr Alexander B Moore, (Fellow), Rochester, Minn, and Dr John T Murphy, (Fellow), Toledo, were elected President-Elect and Secretary, respectively, of the American Roentgen Ray Society at its annual meeting in Toledo, December 6

Dr Henry A Christian, (Fellow), Boston, delivered the annual lecture at the Scripps Metabolic Clinic at La Jolla, Calif, January 25, on "Chronic Nonvalvular Heart Disease Its Causes, Diagnosis and Management"

Dr Charles A McKendree, (Fellow), New York, has been appointed Assistant Professor of Clinical Neurology in the College of Physicians and Surgeons of Columbia University

Dr Aldred Scott Warthin, (Master), delivered the De Lamar Lecture on "The Incidence of Latent Syphilis in the Population," at the School of Hygiene, Johns Hopkins University Medical School, on Tuesday, January 21, 1930

Dr William D Sansum, (Fellow), Santa Barbara, Calif, has become a Life Member of the American College of Physicians, as of January 1, 1930, by subscription of the Life Membership Fee to the College Endowment Fund

Dr Wilfred M Barton, (Fellow), Washington, D C, appeared on the program of physicians presenting a series of clinics at the University of Maryland, Division of Medical Extension, Baltimore, Maryland, on

Thursday afternoons during January and February of 1930

Dr Henry J John, (Fellow), Cleveland, Ohio, is the author of an article, entitled "Problems in Diabetes," printed in the Journal of the Oklahoma State Medical Association, January, 1930

Dr Edgar V Allen, (Associate), Rochester, Minn, has been in Europe since April of 1929 pursuing undergraduate work He studied two months at the Medizinische Universitäts Klinik at Leipzig under the supervision of Professor Morawitz, Director of the Klinik During Dr Allen's work at the Klinik, he received an appointment as Fellow of the National Research Council

From Leipzig, he visited, with Dr C H Mayo, the medical clinics in Berlin, and then went to Zurich, Switzerland, for three weeks' visit to the clinics there In August, 1929, he went to Munich, where he has been working with Geheimrat Professor Friedrich von Muller in Medicine and with Geheimrat Professor Borst in Pathology More recently, Dr Allen has been working in Forschung Anstalt fur Psychiatrie He has also visited the clinics of Paris, Prague and Vienna He plans to go to London to study with Sir Thomas Lewis during the months of May, June and July of 1930, and return to America during August

The following gifts of publications by members of the College are acknowledged

Dr Curran Pope, (Associate), Louisville, Ky, Book, "Practical Hydrotherapy"

Dr Miles J Breuer, (Fellow), Lincoln, Nebr, Reprint, "The Present-Day Conception of Tuberculosis"

Dr Ralph O Clock, (Fellow), Pearl River, N Y, Reprints "The Use of Normal Horse Serum for the Treatment of Burns" "Hay-Fever and its Treatment with Clycerolated Pollen Antigen"

Dr Oliver T Osborne, (Fellow), New Haven, Conn, Reprint, "Mouth Infection"

Dr Walter M Simpson, (Fellow), Dayton, Ohio, Reprints

"Primary Chondroma of the Lung"

"Tularemia (Francis's Disease)"

- "Tularaemia (Francis' Disease)"
- "Tularemia—Study of Rapidly Fatal Case"
- "Tularemia (Francis' Disease)—A Clinical and Pathological Study of Forty-Eight Non-Fatal Cases and One Rapidly Fatal Case, with Autopsy, Occurring in Dayton, Ohio"
- "A Clinical and Pathological Study of Fifty-five Malignant Neoplasms of the Thyroid Gland"
- "Tumor-Thrombosis of the Inferior Vena Cava with Four Additional Cases of Neoplastic Invasion"
- "Aberrant Pancreatic Tissue—An Analysis of 150 Human Cases with a Report of a New Case"
- "Tularemia (Francis' Disease)—Report of Four Additional Cases"
- "Three Cases of Thyroid Metastasis to Bones"
- "Graves' Constitution (Warthin)"
- "Diffuse Vertebral Metastasis of Prostatic Carcinoma Without Bony Changes"
- "Actinomycosis of the Vertebrae (Actinomycotic Pott's Disease)"
- "Tularemia (Francis' Disease) A Clinical and Pathological Study of Sixty-one Human Cases Occurring in Dayton, Ohio"
- "Tularemia (Francis' Disease) Experiences with Fifty-three Cases Occurring in Dayton, Ohio"
- "The Surgical Pathology of Graves' Disease, With Special Reference to Its Prognostic Significance"
- Dr Carl V Vischer, (Fellow), Philadelphia, Pa, Reprints
- "Acute Miliary Tuberculosis Report of Cases with Recovery"
- "Report of Arthritis Conference, Hahnemann Hospital"
- Dr William C Voorsanger, (Fellow), San Francisco, Calif, Reprint, "Vaccine Therapy in Infectious Bronchitis and Asthma"
- Dr Coursen B Conklin, (Fellow), Washington, D C, Reprints
- "Diagnostic Problems Peculiar to Pediatrics, with Special Reference to Child-Parent Psychology"

- "Infant Feeding"
- "Congenital Atresia of Bile Ducts"
- "Aspiration of Stearate of Zinc Powder in Infancy."
- "Acute Primary Pneumonia"
- "Some Observations on the Correlation of Physical Findings in the Chest in Infancy with Pathology"
- Dr Frederick J Farnell, (Fellow), R I, Reprint, "The Individual's Responsibility and The State's Responsibility"
- Dr Lorenz W Frank, (Fellow), Denver, Colo, Reprints
- "Tuberculosis and Goitre"
- "The Basal Metabolism in Pulmonary Tuberculosis"
- "Rheumatic Fever"
- Dr Philip B Matz, (Fellow), Washington, D C, Reprint, "The Surgical Treatment of Pulmonary Tuberculosis in the United States Veterans' Bureau"
- Dr John A Murphy, (Associate), Philadelphia, Pa, Reprint, "Pollen Suspensions A Preliminary Report"

#### PLACEMENT SERVICE

The Executive Offices have on file a few physicians who are seeking new appointments. Some of these are Associates or Fellows of the College. There are at present one well qualified Internist and one Radiologist, who are seeking new connections with Fellows of the College who desire assistants.

The Executive Offices serve as a sort of clearing house through which members of the College may seek assistants, or may seek new connections. The College will assist in securing authentic information, but cannot assume responsibility in connection with recommendations. The purpose of the Executive Offices is to serve the membership in the best possible way. Inquiries are invited.

Attention of members of the American College of Physicians is called to the following Fellow who is desirous of making new connections. Correspondence should be addressed to the Executive Secretary, E. R. Loveland, 133-135 S 36th Street, Phila-

delphia, Pa, mentioning the number preceding the following announcement

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## OBITUARY

Dr Harry Monroe McClanahan, (Fellow), Omaha, Neb., died November 20, 1929, aged 73

Dr McClanahan, a Pediatricist, received his early education at Monmouth, Illinois, and later took his A B Degree in 1875. He attended the Jefferson Medical College of Philadelphia, graduating with the degree of Doctor of Medicine in 1878. He was resident physician at Jefferson Hospital, Philadelphia, 1878-79, practiced at Alexis, 1879-80, was agency physician at Ft Belknap, Montana, 1880-81, practiced at Woodhull, Illinois, 1881-89, and went to Omaha, Nebraska, in 1889. He had been Professor of Pediatrics at the Omaha Medical College (now the University of Nebraska College of Medicine) since 1892, being made Professor Emeritus in 1927, although he continued to hold clinics and to lecture to the senior class up to the time of his death.

Dr McClanahan was an ex-Vice-President and Chairman of the Section on Diseases of Children of the American Medical Association, a member of the American Pediatric Society, the American Society for Study and Prevention of Infant Mortality, the American Teachers of Diseases of Children (President, 1914-15), Nebraska State Medical Society (President 1901), Douglas County Medical Society (President, 1912), and had been a Fellow of the American College of Physicians since 1920.

He was also a member of the following fraternities: Phi Delta Theta, Phi Rho Sigma and Alpha Omega Alpha.

Dr McClanahan's life was a very active one from the time he graduated in medicine; he was always endeavoring to impart the knowledge of his observation and work to others. He was a regular attendant at the meetings of the various national societies, and endeavored throughout his life to keep up with the present trend of medicine. When others took vacations, Dr McClanahan spent his time at the various clinics of medical societies and abroad to further his education along the lines of advanced science.

Dr McClanahan's first article "The Practice of Medicine Among the Indians" was published in 1881 in the Medical and Surgical Reporter, Volume 44, Washington, D. C. During succeeding years he contributed more than fifty articles dealing with pediatric problems in various national journals. His last publication, written in his seventieth year, was a book entitled "Pediatrics for the General Practitioner," published January 1, 1929, by the J. B. Lippincott Co.

Dr McClanahan's sterling qualities, personality and kindly deeds endeared him to all members of the medical profession as well as to the parents and children whom he had the privilege of having under his care and observation.

—Supplied by Dr J. A. Henske, Omaha, Nebraska

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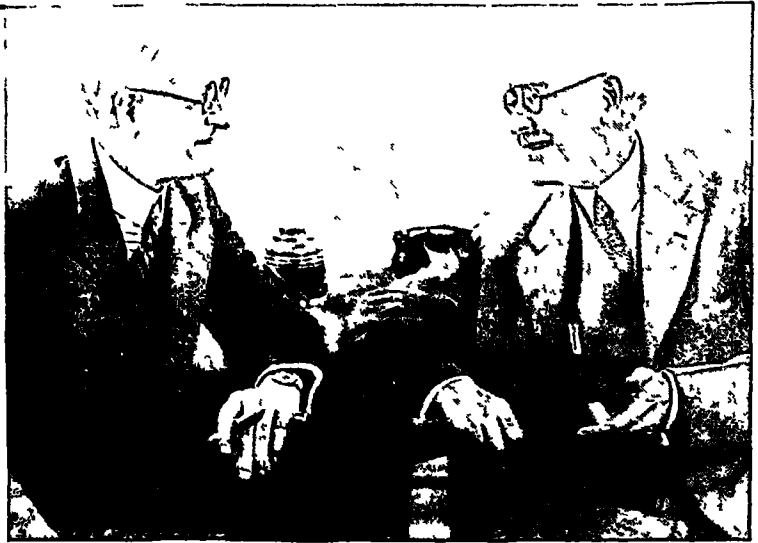
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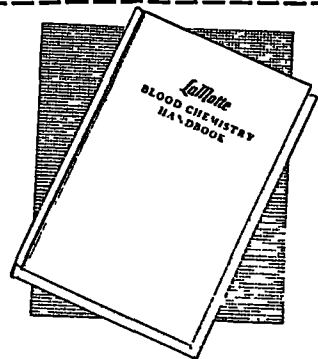
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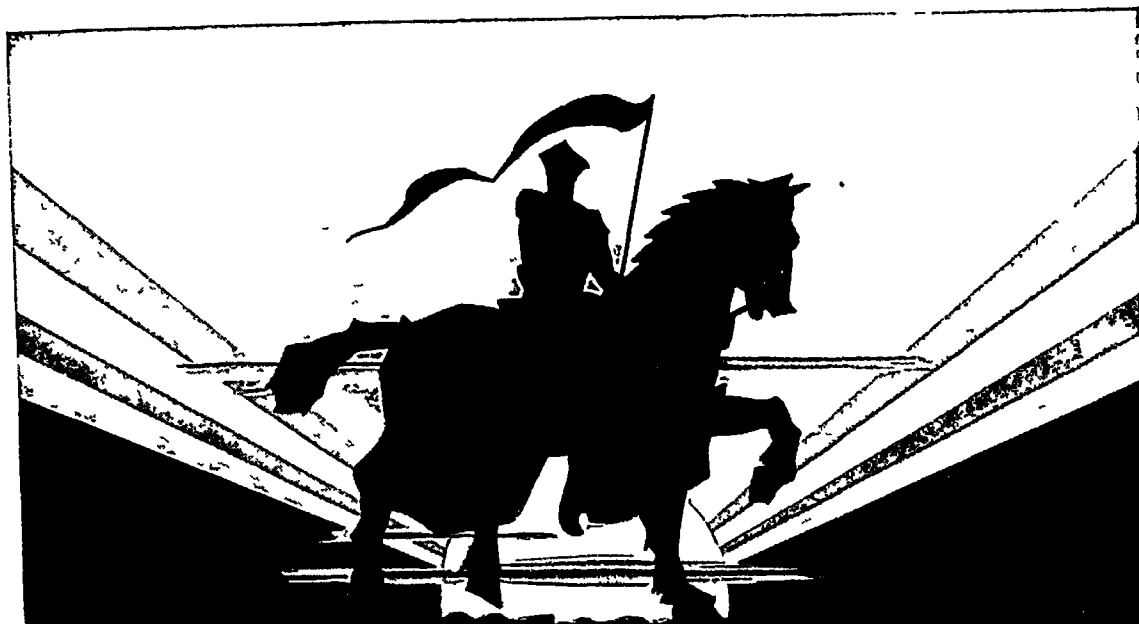
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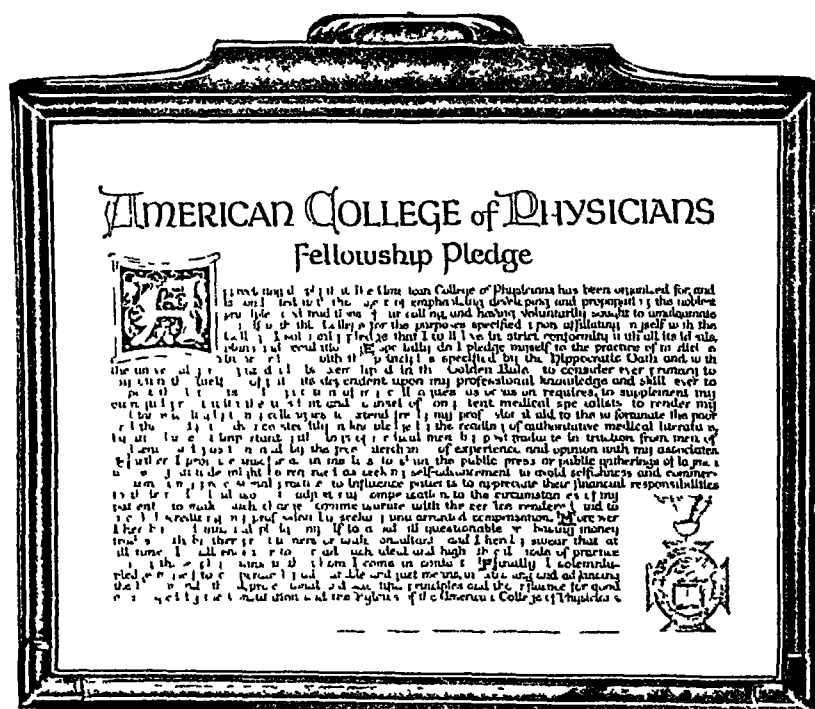
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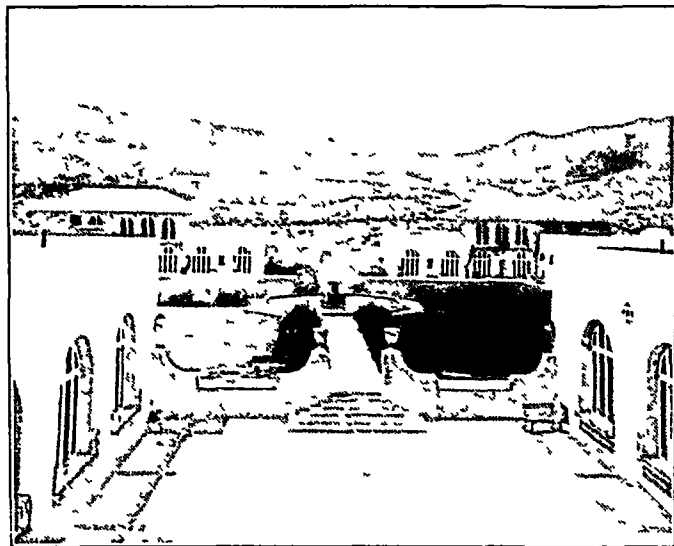
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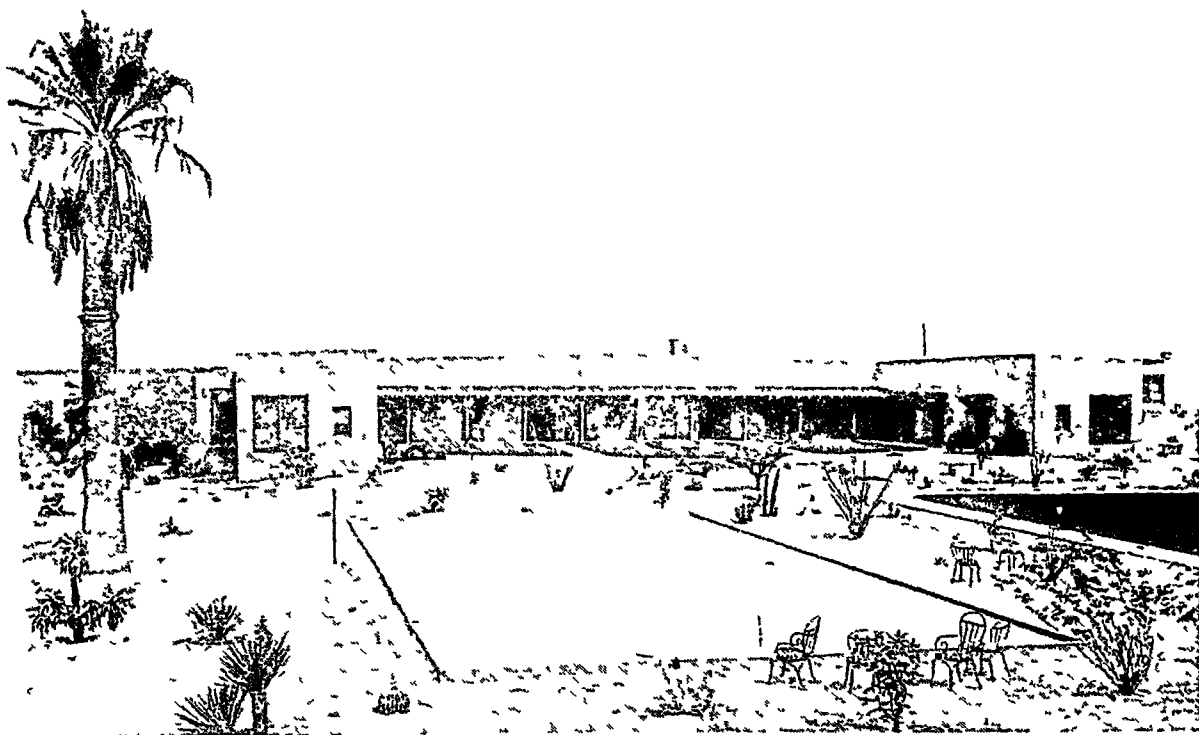
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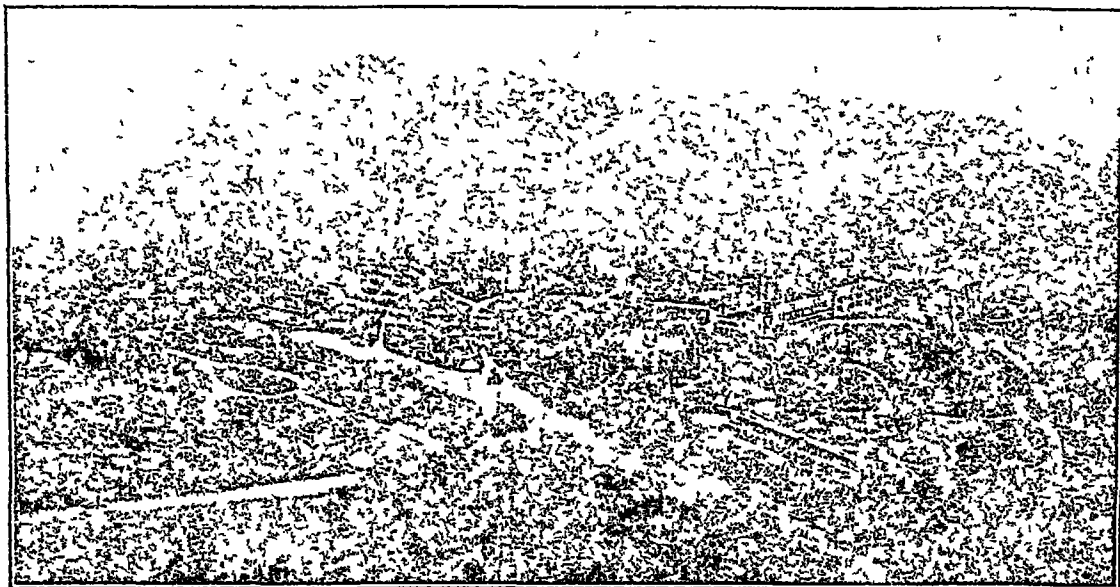
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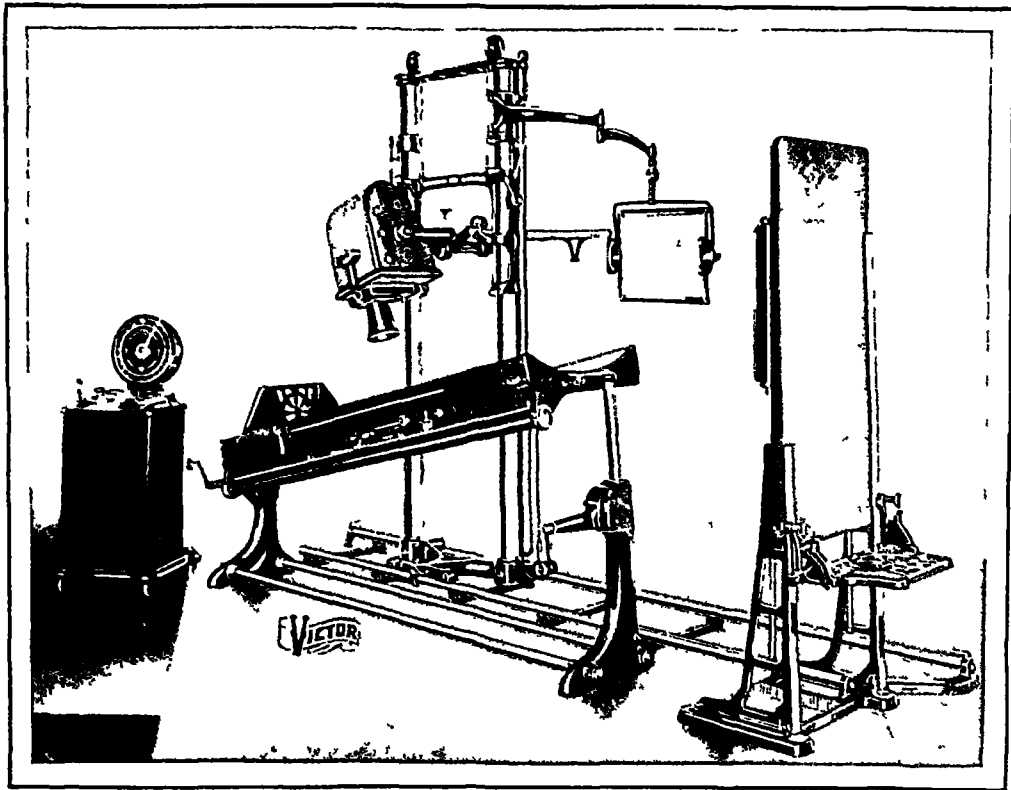
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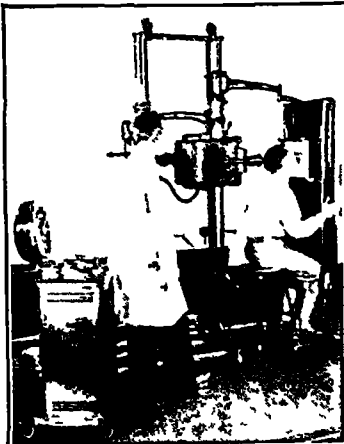
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# Herpes Zoster and Angina Pectoris

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and  
ALBERT S. HYMAN, M.D., F.A.C.P., *New York, N. Y.*

FROM a clinical point of view Herpes Zoster may be readily confused with Angina Pectoris, especially when it occurs in the middle age periods. Mackenzie has pointed out that herpes zoster which develops as a result of ganglionic disturbance of the first four upper thoracic segments of the spinal cord may resemble in every respect the rather characteristic syndrome seen in true angina pectoris.

Other authors have found a very close association between herpes zoster and angina pectoris of the neurogenic type. Some have stated that the two diseases are manifestations of the same etiologic background, while others believe that angina pectoris may be the result of herpes zoster itself. The situation is further complicated by the fact that herpes zoster may follow after an attack of angina pectoris. A consideration of these apparently contradictory opinions may be due in part to the fact that the pathways concerned in the neurogenic arc utilized in both conditions may be the same.

There have recently been many demonstrations of the nerve pathways involved in carrying the pain sensations in angina pectoris. Several authors have been able to point out zonal areas of the skin which are directly

associated by complex neuron connections with the cardiac plexus and the ganglionic elements themselves. Angina pectoris of the neurogenic type must be sharply differentiated from the anginal seizures which are the result of stenocardia, whether of the functional or of the degenerative coronary arterial type. In this latter group considerable pathology of the heart is usually found, coronary thrombosis, myocardial infarction, sclerosis and aneurysm of the heart or great vessels are common postmortem findings.

Angina pectoris of the neurogenic type, on the other hand, presents no such changes in the heart. Indeed, the heart may be entirely "normal" in cases which have clinically had frequent severe anginal seizures. Every pathological laboratory can demonstrate three types of cardiovascular change: first, those who had a history of anginal attacks with extensive coronary arterial change; second, those with a similar history but with normal hearts and blood vessels; and third, those without anginal history with marked coronary and myocardial disease. Cabot, for example, in a series of 138 cases had 33 cases of the first group, 11 of the second, and 94 of the third. There is apparently thus no close connection between the intensity and severity of the

anginal seizures and the pathologic physiology occurring in the cardiovascular system

Probably no subject has been as fruitful of academic speculation within the past decade as the anginal syndrome. The bibliography is replete with innumerable theories in regard to the various phenomena associated with this condition. In the last analysis, however, very little of fundamental importance has been added to the original description by Heberden and to the theory of its cause by coronary involvement described by Jenner in his memorable letter to Heberden concerning Hunter's illness. All this transpired at the close of the eighteenth century, and in the 200 years which have followed, neither of these observations has been materially shaken. Important contributions have, however, been made by Allbutt, Vaquez, Potain, Mackenzie, Stokes, Wenckebach, and Danielopolu which have clarified this difficult clinical syndrome.

The division of the anginal picture into the stenocardial and neurogenic types has received almost universal acceptance, confusion still exists in regard to the association between these two groups and also in regard to the development of the stenocardial group from the neurogenic type. In this connection, we have been interested in a series of cases which have clinically been diagnosed as herpes zoster and which subsequently developed a characteristic stenocardial picture and died from coronary artery disease with its associated myocardial breakdown. Three of these cases were followed closely over a period of five years, they were seen first during or imme-

diately after an attack of shingles. They were studied from a cardiovascular angle, not because of the herpes zoster, but because they had been complaining of heart consciousness.

At the time of the first examination rather normal cardiovascular findings were noted, electrocardiographic tracings, X-ray examination, blood pressure readings, vital capacity estimations, and function tests were made. In periods varying from six months to three years, these patients began to suffer from typical anginal seizures of varying degrees of severity. Detailed cardiovascular surveys made from time to time showed the onset and progressive nature of certain vascular degenerative changes. Two of the cases had more than two attacks of herpes zoster, but all three of the cases retained and exhibited the tender points of the head zonal areas described by Mackenzie. A detailed description of each case is presented below.

Case 1 B P, Age 54. Was seen on November 3, 1923. Her previous cardiovascular history was essentially negative, her family physician had known her for about 20 years during which time he had treated her only for her pregnancies and once for influenza. During the latter part of October, 1923, she began to complain of sharp burning pain in the left chest, especially in the axillary line. The pain was very severe, the family physician x-rayed her chest suspecting a pleurisy but the roentgenograms were negative. The heart in this picture was rather normal for this age period. In about ten days the characteristic skin lesions of shingles broke out. The patient was carefully examined for possible foci of infection, and one abscessed tooth was removed. Shortly after this the patient complained of palpitation and dyspnea and was referred to us for cardiovascular study.

When seen on November 3, 1923, she



still had five small skin lesions located in the midaxillary line at the level of the fourth and fifth ribs. The skin over this entire area was hyperesthetic. Electrocardiographic studies showed rather normal tracings (Figure 1A). There was a sinus rhythm with a moderate left axis deviation of the heart which at this age period may be considered as normal. Her other tests were also normal for this age group.

The skin lesions of herpes zoster slowly cleared up and disappeared in about six weeks. The patient was seen again on October 17th, 1925. In the two years which had intervened she had had three separate attacks of herpes zoster, all on the left side and all within the head zone areas supplied by the three upper thoracic ganglia. The last attack occurred during April, 1925. During that summer she began to experience substernal discomfort on exertion and twice she had what appeared to be true anginal seizures with pain which radiated down the left arm to the elbow.

Cardiovascular examination made at this time (Figure 1B) showed in addition to a more marked left axial deviation of the heart alterations of the T-waves in the second and third leads. Orthodiagraphic X-ray examination indicated a slight increase in the diagonal diameter of the cardiac shadow. Her blood pressure remained the same. A diagnosis of coronary artery disease was made and the patient was placed on moderately large doses of diuretin after the method described by Moon at the National Hospital for Heart Diseases in London.

The patient continued to have her anginal seizures and except for a few months' remission during the spring of 1926 she continued to suffer from stenocardial attacks even upon the slightest exertion. She was seen from time to time during the next year and a half. Repeated electrocardiographic tracings showed the development of coronary sclerosis and, finally on March 6th, 1928, she was seized with an attack which was diagnosed as coronary thrombosis with infarction. She remained in this status anginosus for about ten days with a slight

rising temperature, moderate leucocytosis, poor and thready pulse, which at times was grossly irregular and suggested either auricular fibrillation or an extrasystolic arrhythmia. The heart sounds for a few days were practically inaudible.

Her convalescence was very slow, she was electrocardiographed on May 21st again (Figure 1C) and a well established auricular fibrillation with left ventricular extrasystoles was found. The orthodiagraphic X-ray showed but slight cardiac enlargement. The tender points in the axilla and down the inner surface of the left arm were still present and the patient frequently complained that even the shoulder straps of her undergarments were at times unbearable on the left side. The patient from this period on did not respond to treatment and on July 10th, after a rather mild attack died before medical attention could be secured.

Case 2 H W, Man, aged 57. Was seen first on September 4, 1925, about three weeks after he had recovered from a very severe attack of herpes zoster. The scars of the lesions could still be seen running in the characteristic zonal fashion along the course of the third, fourth, and fifth ribs on the left side. The skin over this area and extending down as low as the sixth interspace was hypersensitive. The patient said that he had been having a "heavy sensation" over the chest for the past week and had been advised to have his heart examined. So far as he knew, he had never had any heart trouble, he had passed an insurance examination about five years before.

Cardiovascular studies showed that he had a blood pressure of 145/95, his heart was normal in size but the aortic shadow was somewhat widened. The heart sounds were of good quality and no murmurs were heard. Vital capacity tests were normal. Electrocardiographic tracings (Figure 2A) were essentially normal for this age period.

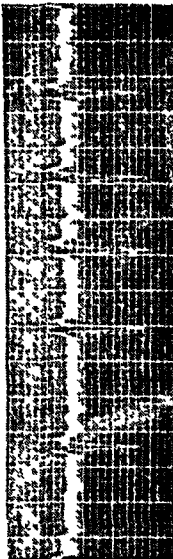
During the summer of 1926 he again had an attack of herpes zoster which, however, lasted only about two weeks. He was not examined at this time as he was in another city, but on October 10th, 1926, he was



LEAD I

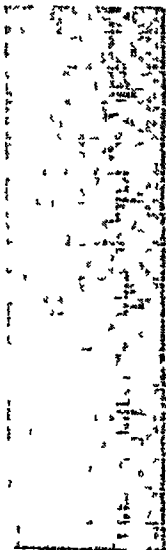


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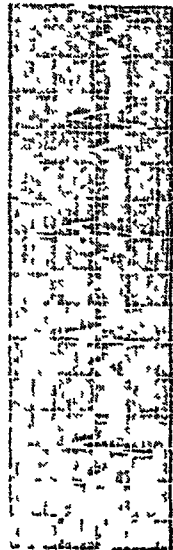


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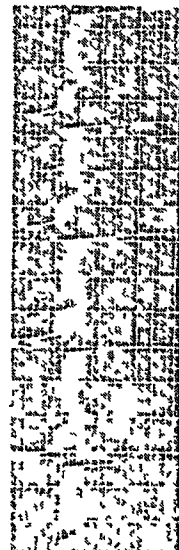
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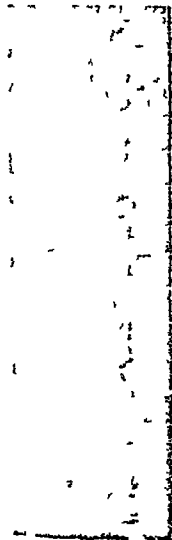


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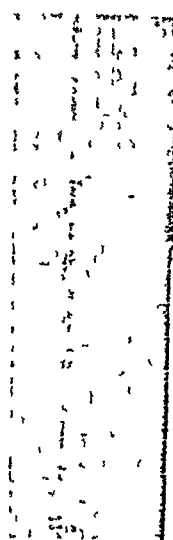
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LEAD I



LEAD II



LEAD III

1C

again studied, he had no complaints except that of insomnia. Even large doses of sedatives failed to produce the desired effect. His physical examination at this time also failed to reveal anything of importance. The electrocardiograms were similar to those taken a year previously.

On February 7th, 1927, during his convalescence from an attack of septic sore throat he experienced his first anginal attack. The pain while not very severe seemed to have localized itself in the same area as that involved by the previous two attacks of herpes zoster. Indeed, the patient himself believed that he was going to have another attack of shingles. It was impossible to examine the patient until about a month later, he was somewhat confused at this time in regard to the pain. He said that it resembled the burning pain of herpes zoster in exactly the same place that he had previously experienced. The pain now, however, seemed to come on in attacks which lasted only a few minutes and which he thought were connected with something which he had eaten, as he usually experienced the pain after breakfast. He had been looking for the skin lesions which he had learned to dread, but they had not appeared. The skin over this area while not as hyperesthetic as previously was still more sensitive than the skin on the right side of the chest.

Examination at this time showed progressive cardiovascular pathology. The heart was considerably enlarged, his blood pressure had fallen to 95/65, and his electrocardiographic tracings (Figure 2B) showed alterations of the T-waves in Leads I and II. He had a normal sinus rhythm. Under a regime of enforced rest, abstinence from tobacco and the giving up of his occupation of traveling salesman he seemed to have improved and was only seen by us again fourteen months later.

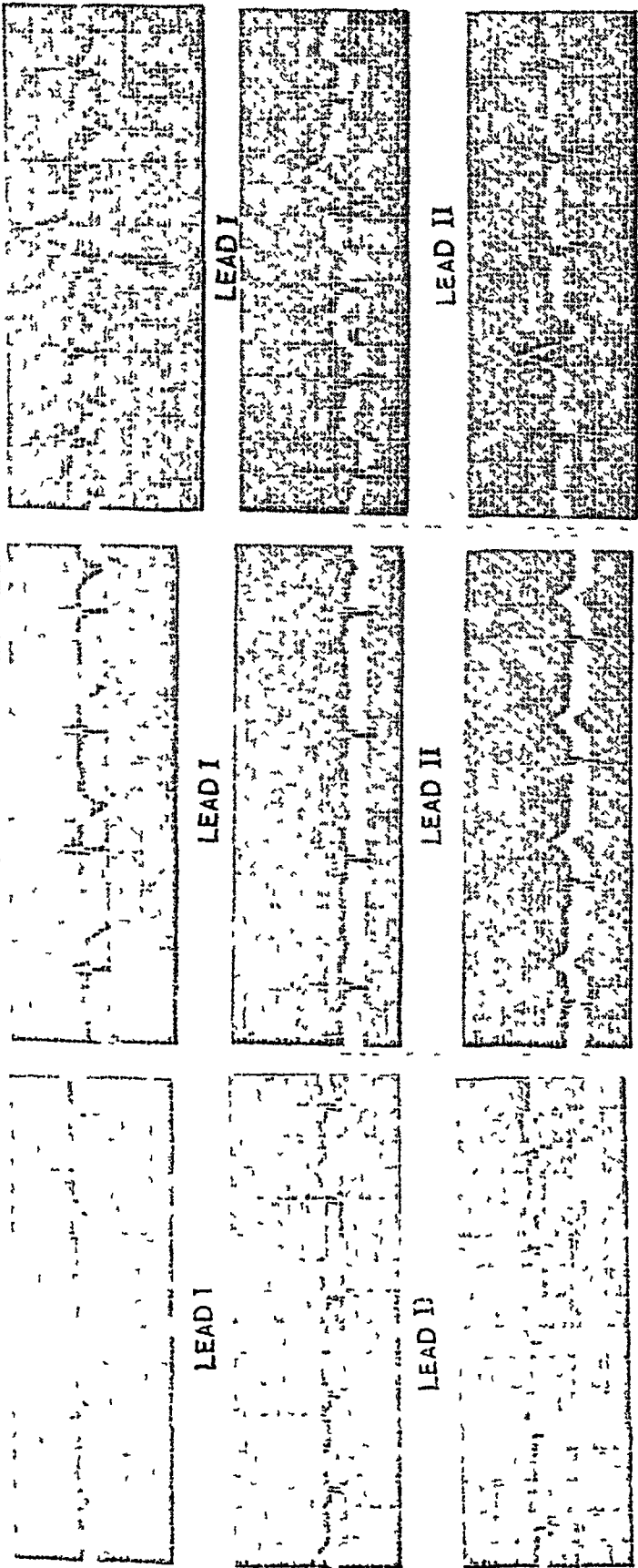
On April 9th, 1928, he returned to the city and was examined again. We were struck with the marked change in the appearance of the patient, he had lost about twenty-one pounds in weight and looked pale, haggard, and drawn. He had been

having repeated anginal attacks and the insomnia which he had suffered in 1926 had returned, he thought that it was due this time to his anginal attacks which occurred even while in bed. He had been using nitroglycerin for some time but with diminishing effect.

Electrocardiographic tracings (Figure 2C) now showed characteristic T-wave alterations in the significant leads, there were also many ventricular extrasystoles arising from different foci. The heart sounds were poor and distant. The patient had relatives in the West and was advised to visit them for a prolonged rest. He was not seen again but we received frequent communications from him. It appears that he did very well symptomatically for a few months. In November, 1928, he had a very severe anginal seizure which confined him to bed for about six weeks. He was said to be in extremis a few times, he rallied, however, and on January the 10th, 1929, he wrote saying that he had almost entirely recovered and was planning to return East. On March 7th, 1929, after a series of anginal attacks, he died suddenly.

Case 3 D K, man, aged 46. Seen for the first time December 7, 1925. He had been annoyed from time to time for the previous six months with peculiar burning pains over the precordium, axilla, and inner aspect of the left arm. He said that he had noted a "rash" at intervals in the same area but paid no attention to it, he had come to believe that these pains were due to his heart and although he had been repeatedly told that his heart was normal, he had developed a cardiophobia.

A complete cardiovascular study revealed nothing of interest. His electrocardiographic tracings (Figure 3A) are presented merely for comparison with subsequent records. The skin over the area complained of showed nothing unusual, no lesions of any kind were seen at that time, skin tests, however, showed a definite hyperesthesia. The patient was not seen again for three years. On November 17th, 1928, he appeared again, he said that he had had two attacks of shingles on the left side, one of



them in the spring of 1926, and another attack in the Fall of the same year. The first attack was apparently the most severe, he had numerous skin lesions, which required six weeks to heal, but occasionally since the second attack he had been having similar pains in the same areas. He noted that in the past few months that the pains would come on while walking or climbing stairs, his occupation was that of insurance adjuster, and he was forced to climb many flights in a course of a day's work. The pains were becoming so severe that it was a question of giving up his work entirely. He said that these pains resembled in many respects the pains which he had suffered during his two attacks of shingles.

Cardiovascular examination revealed no great change either in the size or contour of his heart, his blood pressure, however, has risen to 160/90, and he had a slight trace of albumin in his urine with a few granular casts. Electrocardiographic tracings (Figure 3B) showed that marked changes had taken place since the last examination. He now showed a marked left axial deviation of the heart with T-wave alterations in first and third leads suggestive of beginning bundle branch block. Under intensive euphyllin therapy and complete rest he seemed to improve symptomatically.

He was not seen again until September 11th, 1929, at which time he presented all the signs of advanced coronary disease. His stenocardial attacks were occurring at irregular intervals and the pain factor was becoming less important than that of the dyspneic one. This case was interesting in that a diagnosis of bundle branch block was made from the suggestive gallop rhythm and doubled apical impulse. The heart was markedly enlarged and electrocardiographic examination (Figure 3C) showed a well established right bundle branch block. The patient's general condition was rather poor and continued to become progressively worse up to his death which occurred on September, 29, 1929.

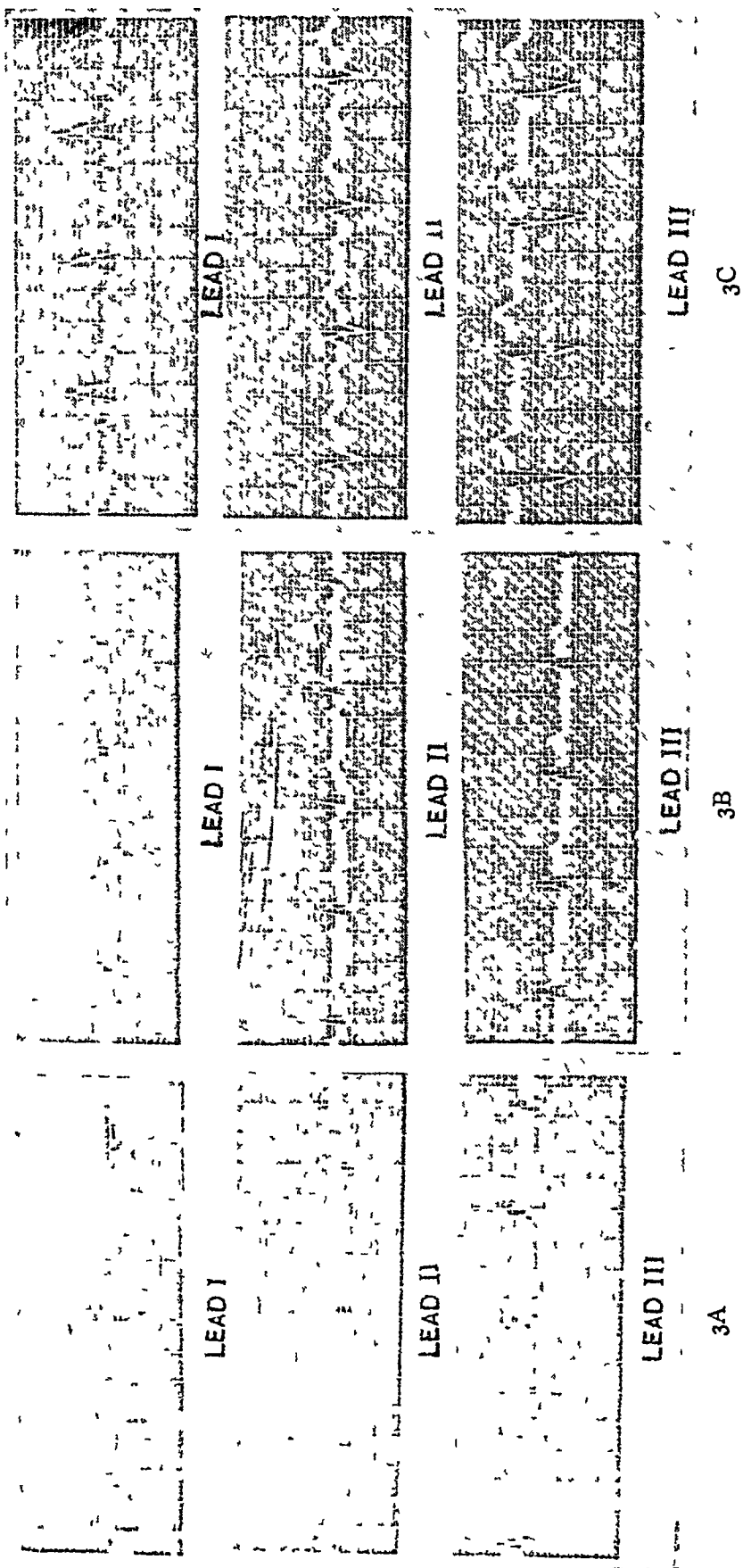
#### COMMENT

These three cases are presented in some detail in order to bring out several factors of interest. The close resemblance between the pain of herpes zoster and that experienced in certain types of angina pectoris is striking, all of the patients remarked upon the similarity in their own description of their symptoms. Two of them could hardly distinguish the difference. This observation is not entirely original, Mackenzie noted it in one of his cases.

In all three of our cases the coronary degenerative changes which took place following the herpes zoster attacks were rapidly progressive and ended fatally within five years. In each of these the herpes zoster occurred at a time when the hearts were apparently still normal and we have had an opportunity to watch the various changes that have occurred up to the time of their fatal termination.

No attempt can be made here to explain the relationship between the development of herpes zoster and the occurrence of angina pectoris in individuals who have subsequently succumbed to coronary arterial disease. The complex neurologic association of the factors involved in the production of herpes zoster appear to have a place in that multiphased clinical syndrome known as angina pectoris.

Whether the pain component of the herpes zoster syndrome and that of angina pectoris is the same, or whether they are two different entities using the same pathways for their transmission is a problem of nice distinction. Our series of cases is too limited to draw any far reaching conclusions but it may serve a purpose in focusing at-



tention upon the possible relationship between the etiologic background of herpes zoster and that of the neurogenic type of angina pectoris

#### SUMMARY

1 Three cases of herpes zoster which subsequently developed angina pectoris and died of coronary artery disease are presented

2 The characteristic burning pain experienced in herpes zoster resembles in many respects that of angina pectoris. Patients may confuse the two

3 Herpes zoster and angina pectoris exhibit identical zonal areas of altered skin sensitivity

4 There is a possibility of a common etiologic background in both herpes zoster and angina pectoris of the neurogenic type

# Poliomyelitis Versus Landry's Paralysis.

## An Attempt to Contrast Their Symptomatology and Pathology,

By HERMON C GORDINIER, A M , M D , F A C P , Troy, New York

THERE is a remarkable difference of opinion among neurologists, internists and epidemiologists, with regard to the identity of Landry's paralysis some contending that the acute ascending or rare descending type of paralysis originally described by Landry is simply a form of poliomyelitis, whereas others contend that Landry's paralysis is an independent symptom complex, not due to the specific virus of poliomyelitis, but due to some unknown form of toxin, bacterial, metabolic or chemic in nature, which seems to have a special affinity for the peripheral motor neurons. With this view, I am inclined to agree, having had the opportunity to observe clinically a large number of cases of poliomyelitis during the various epidemics which have occurred in this country, a few with autopsies, and have also had the rare opportunity of studying seven typical cases of the acute ascending paralysis of the type of Landry, in three of which I was able to make complete autopsies and study the entire nervous system of each.

I will, therefore, by means of photomicrographs attempt to contrast the neuropathology of the two diseases.

\*Read at the Annual Meeting of the Rochester County Medical Society, November, 1928

*Poliomyelitis* Poliomyelitis is really a misnomer and equally so the name given to the disease by Heine, essential infantile paralysis, as the disease is not strictly limited to the motor neurons of the ventral gray columns of the spinal cord or is it by any means confined to infants or very young children, it affects older children and adults in from 10% to 15% of the cases. A definition more in accord with recent scientific investigations is the following: the so called infantile paralysis is a wide spread, acute infectious communicable disease of the nervous system, a meningo-myelo-encephalitis, probably due to a specific, ultramicroscopic, filterable "globoid" body, discovered by Flexner and his co-workers, which has a special predilection for the cells of the ventral gray columns of the spinal cord, the bulbo-pontine cranial nerve nuclei, the cerebral and cerebellar cortex, and rarely the peripheral nerves. Wickman classifies the disease into the following types: the abortive common, spinal type, the bulbo-pontine and Landry's type, the cerebral type of Strumpell, the cerebellar type with acute cerebellar ataxia and the neuritic type.

A number of epidemics have occurred in this country, the first one of which accurately studied, was described



by Dr. Caverly of Rutland, Vermont, in 1894 and occurred in the Rutland Valley. He reported about 132 cases. During this epidemic, I saw two cases, both in adults, which because of the meningeal involvement, delirium and coma, I made a probable diagnosis of cerebro-spinal meningitis, until the residual paralysis and subsequent atrophy, made the diagnosis of the cases perfectly simple.

Subsequent epidemics occurred in 1907 and 1908 in New York, Vermont, Wisconsin, Pennsylvania, Minnesota, Michigan, Virginia and Nebraska. It is very probable that these epidemics may have been due to a large contingent of immigrant carriers from Scandinavian countries, where the disease existed during the early spring and summer.

The great epidemic of 1916 with which most of you are familiar seemed to have originated in Boston and greater New York, particularly in Brooklyn, and to have been carried along the lines of travel throughout Massachusetts and New York and the rest of the New England and Middle States, affecting about 30,000 people. Several small epidemic recurrences have occurred in various urban and suburban districts ever since, and sporadic cases are not at all rare.

I will not detain you with a detailed description of poliomyelitis but will describe its chief symptoms together with those of Landry's paralysis as observed in the seven cases of the latter disease which I have studied.

*Landry's Paralysis.* All of the seven cases of Landry's paralysis were in adults, varying in age from 28 to 50 years. The disease came on sud-

denly first a rapidly ascending flaccid paralysis beginning in the lower extremities and rapidly involving in turn the muscles of the legs, thighs, pelvis, trunk, upper extremities, diaphragm, chest, neck, throat, head and cardio-respiratory centers, with death in five from cardio-respiratory paralysis. \*In two cases, in which complete and permanent recovery occurred, the patients' symptoms were as described above and they both developed marked bulbar symptoms. In both of these cases complete physiological restitution of all the paralyzed muscles occurred without the slightest evidence of residual paralysis, muscular atrophy, reaction of degeneration, deformities or other evidences of trophic disturbances. In none of the cases were there any objective sensory disturbances found. In two cases, slight prodromata occurred, such as malaise, sore throat, pains and aches in the extremities and paresthesia. The mind was clear in each case until the last. There were no cranial nerve involvements except those of the bulbar nuclei. There was slight febrile reaction in two cases at the onset, in the others, none existed until just a day or two prior to death. The organic reflexes were controlled, the deep reflexes as well as the superficial reflexes were absent. The spleen was just palpable in two cases, no lymph nodes were palpable in any case.

The picture presented by a typical case of Landry's paralysis is very striking. The patient assumes an extreme dorsal decubitus, is unable to sit up, turn to one or the other side or to

\*Albany Med. Annals, January, 1904.

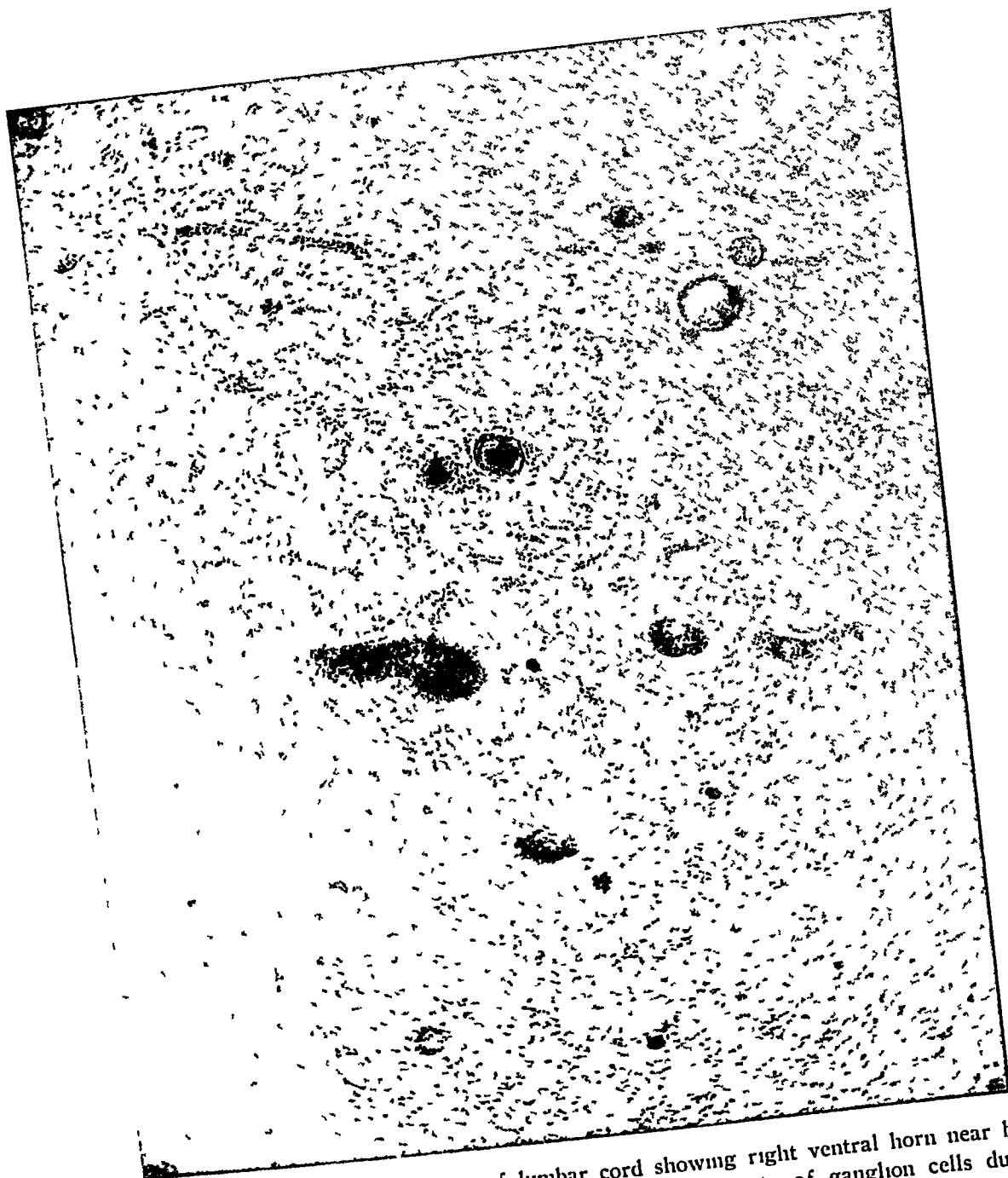


FIG. 1—*Polioomyelitis* Section of lumbar cord showing right ventral horn near base, with interstitial and perivascular infiltration. Note the paucity of ganglion cells due to edema and cuff of round cells surrounding vascular walls. Low power.

rotate, extend or flex the head. The complete flaccid paralysis of all four extremities, great difficulty in swallowing and articulation, marked dyspnea from involvement of the respiratory and cardiac centers, retention of perfect consciousness to the last with facies of extreme anxiety and apprehension, completes the sad picture of this dreaded disease.

*Poliomyelitis* The paralytic manifestations of poliomyelitis are often preceded by prodromata such as sore-throat, coryza, a slight, moderate or high febrile rise, rapid pulse, diarrhoea, vomiting, rarely convulsions, severe headache, neuralgic or rheumatoid pains, profuse sweating, soreness of the muscles of the neck, back or extremities, hyperesthesia, severe abdominal pains, two cases seen in consultation were at first diagnosed as appendicitis until the sudden onset of paralysis made clear the diagnosis. Vertigo, apathy, drowsiness often approaching coma, tremor of extremities, paresthesia, stiffness of the neck on bending forward and occasionally definite Kernig sign. In the abortive type of poliomyelitis, the prodromata may be the only symptoms present or they may be associated with pallor, slight temporary weakness, together with slight diminution or loss of the deep reflexes of one or more of the extremities. The type and character of the motor symptoms are entirely dependent on the longitudinal extent and exact situation of the pathologic lesion. The paralysis usually comes on rapidly following the prodromata, and there may be complete or partial paralysis of a limb, or two or more limbs, with loss of the deep reflexes. Occasionally,

if the lesion is very limited, a single group of muscles may be involved, such as the erector spinae, abdominal muscles or those of the throat, face or those innervated by the ocular nerves, upper or lower arm or peroneal group, or rarely only a single muscle may be affected, so localized may be the inflammatory process. I have twice seen just the deltoid muscle involved, and once the quadriceps extensor femoris. The paralysis is usually of the flaccid type and it is followed in a week or two by definite muscular atrophy with the electrical reaction of degeneration, vasomotor and trophic symptoms are quite common such as pallor, localized sweating, lividity and coldness of the skin of the affected parts, marked muscular atrophy, and in children the growth of the bones of the extremities is often retarded and changes in the size of the lumen of the blood vessels not infrequently occur. The reflexes in the preparalytic stage may be exaggerated, diminished or absent on one or both sides, depending on the extent and exact location of the lesion. In the rare cerebro-cortical or upper motor neuron type described by Stumpell, the paralysis is of the spastic type, hemiplegic in distribution, the deep reflexes are exaggerated and certain pathologic reflexes are present such as the Babinski, Oppenheim, Gordon and Shattuck reflexes as well as ankle and knee clonus on the paralyzed side. The paralyzed muscles are stiff and rigid. Subjective sensory manifestations are rather common, objective sensory findings other than muscle or nerve tenderness and slight neck stiffness, are rare. Examination of the spinal fluid should be carried out in every



FIG. 2—*Poliovirus*. Section through right ventral horn of lumbar cord showing interstitial round cell infiltration, polyblasts and degenerated ganglion cells. High power.

suspicious case, not only because of the help it may lend in the early diagnosis of the preparalytic or abortive type of case, but also as a guide to the early introduction of immune serum

In order to make clear the neuropathology of polomyelitis and Landry's paralysis, I will contrast the changes found in the nervous system in a case of each disease \*

#### CASE I

A case of acute polomyelitis of the Landry type in a young adult, involving almost simultaneously the muscles of both upper extremities, trunk, diaphragm and those of the left lower extremity. Death at the end of five days from respiratory paralysis

The post mortem examination was confined to the central nervous system. The dura was normal, sinuses free. The pia arachnoid showed increased vascularity. No exudate observed. There was an increase of the cerebro-spinal fluid. Otherwise, the brain appeared normal.

*Spinal Cord* The membranes of the spinal cord were deeply injected and there was an increase of cerebro-spinal fluid. The spinal cord on section showed in the region of the central gray matter, remarkable increased vascularity, which gave that region a deep purple or velvety appearance, thus making the letter 'H' stand out clearly in sharp contrast to the surrounding white matter.

#### MICROSCOPIC EXAMINATION

*Spinal Cord* The most obvious change is a remarkable perivascular and interstitial round cell infiltration universally distributed throughout the spinal cord, being most marked in the cervical and lumbar regions. While this infiltration is particularly striking in the ventral gray columns, it is not confined to these regions as it exists to a

lesser degree in the posterior gray columns and surrounding white matter. The pia mater, especially that portion covering the ventral surfaces of the cord and medulla, shows both a diffuse and vascular mononuclear round cell infiltration. Many of the centripetally coursing vessels, supported by the delicate sub-pial neuroglia septa, show marked perivascular infiltration. The dura is normal throughout. The central canal seems enlarged and contains a number of small round cells. The motor cells of the ventral gray columns especially those of the cervical and lumbar segments, are greatly reduced in numbers, which is explainable by the accompanying inflammatory edema. They all show various degrees of degeneration, from slightly early chromatolysis to absolute destruction, and many cells are the seat of an active neurophagocytic process. The blood vessels, especially of the central gray matter, are dilated and full of blood corpuscles. No thrombi or capillary hemorrhages found. The round cell infiltration is chiefly of the lymphocytic type, with small deeply stained nuclei, with non-granular protoplasm, diffusely scattered through the gray matter are a number of larger cells with granular protoplasm, they may be polyblasts or glia cells. The ventral or dorsal nerve roots show no definite change.

The Weigert stain shows no degeneration of the fibres of the white columns of the cord. Considerable separation of the fibres existed, however, as if from the compression of edema. Similar changes, although not as pronounced, existed in the medulla and pons, especially in the region of the cranial nerve nuclei and pia.

The cerebellum appeared normal. The para-central lobules show both a diffuse and vascular, round cell infiltration. The large pyramidal cells of the motor cortex show no pronounced alterations.

#### CASE II

A case of rapidly ascending motor paralysis of the type of Landry, which began suddenly in the muscles of the lower extremities, extended rapidly upward, involving in turn those of the thigh, pelvis, trunk, spine,

\*These cases were reported in full together with bibliography to date in a paper before the Amer. Neur. Ass., May 1914.

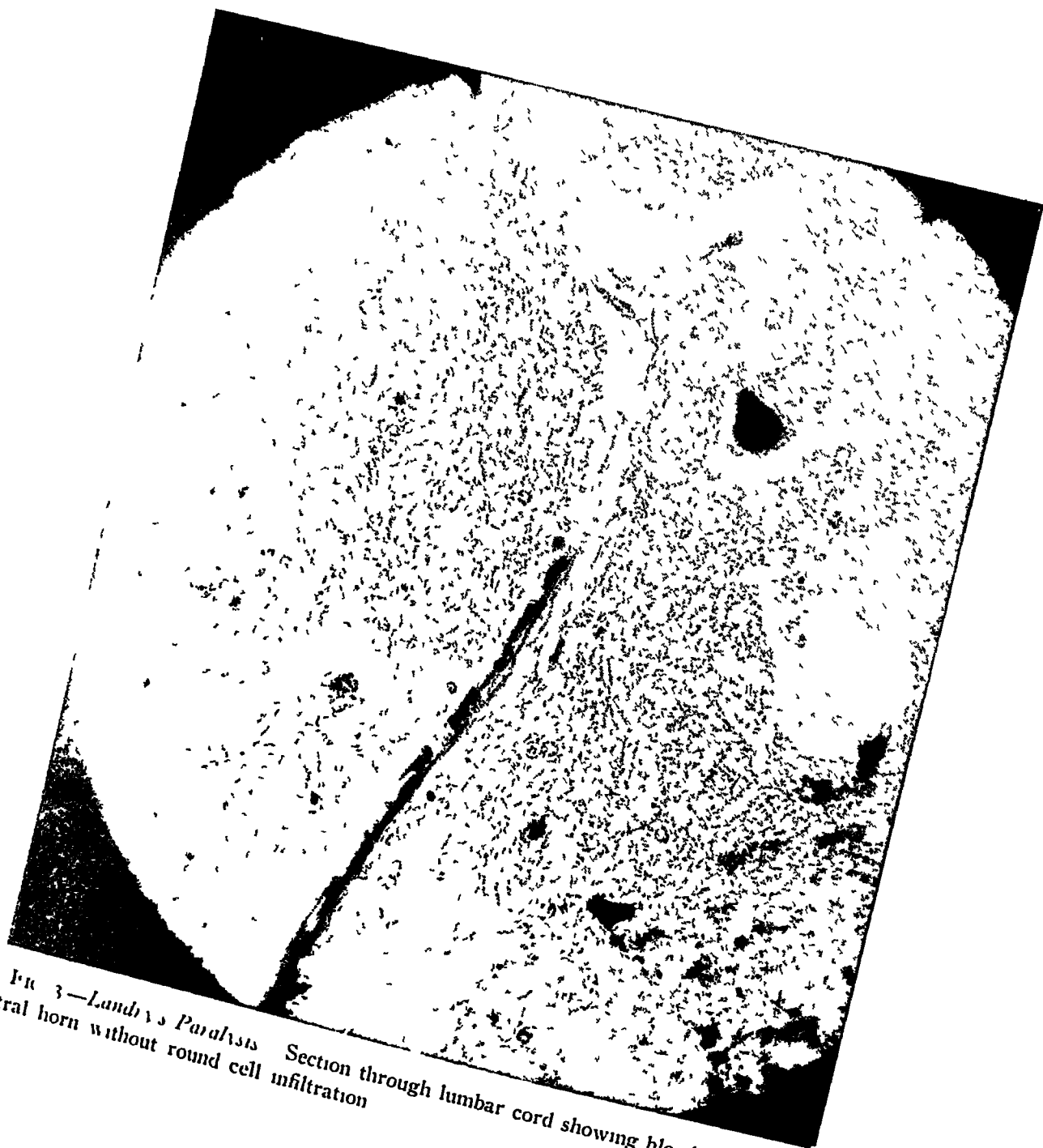


FIG. 3—*Landolt's Paralysis* Section through lumbar cord showing blood vessel in right ventral horn without round cell infiltration

upper extremities and diaphragm, and without subjective or objective sensory disturbances, the mind being clear to the last. Death from respiratory paralysis eight days from the onset.

### **PATHOLOGY OF LANDRY'S PARALYSIS**

**Bram** The skull and scalp show no change. The dura is free and is otherwise negative. No thrombi exist in the sinuses and no general congestion is present. The pia arachnoid seems perfectly normal, as does the whole cerebral cortex and base. The blood vessels of the brain show no changes. The brain stem, pons, medulla, cerebellum and spinal cord appear negative, macroscopically. The spinal cord, pons and medulla, show no macroscopic changes on section. Cultures taken from the cerebrospinal fluid, heart's blood, brain, spinal cord, spleen and liver show no growth.

Sections were made from various levels of the spinal cord, medulla and motor cortex and stained with hematoxylin and eosin, neutral red, Nissl's, van Gieson's and the Weigert-Pal methods. The membranes of the cord and brain were normal. The small blood vessels of the ventral horns and intermediate gray matter were unusually prominent, many were dilated and contained thrombi. There was no definite perivascular or pericellular mononuclear infiltration. The vessel walls appeared normal. Very slight round celled infiltration existed throughout the central gray matter and about the slightly dilated central canal, there was a great paucity of cells about the blood vessels. Scattered throughout the central gray columns of the entire spinal cord, but especially prominent in sections through the lumbar and cervical segments were multiple small capillary hemorrhages. The ventral column cells at all levels, but especially those of the lumbar and cervical regions showed distinct degenerative changes. Many of the cells appeared swollen, irregularly shaped with their chromatin network deeply stained or very granular and pale. Some cells showed marked central chromatolysis with the peripheral granules intact, whereas others showed both central and

peripheral chromatolysis with displaced nuclei, whose nuclear envelopes were wavy or irregular in outline and some showed distinct fragmentation. A few cells devoid of their nuclei and their Nissl bodies were degenerated into a fine dust. The normal pigmentary substance or lipoid of the cells was greatly in excess. Many shadow cells existed with absent nuclei and with only a few scattered degenerated tigroid bodies. Some of these cells contained leucocytic inclusions and rested in dilated pericellular spaces, while the dendrites were for the most part preserved. Some cells were devoid of them, and there was in many of them a paucity of the Nissl bodies. Very slight chromatolytic changes existed in a few of the cells of Clark's column. They were, otherwise, normal as were the cells of the posterior gray columns and those of the posterior spinal ganglia. The ventral nerve roots showed slight degenerative changes doubtless secondary to the changes in the cells of the ventral cornua. The posterior nerve roots were normal. The intracornual nerve network appeared normal. Sections through the motor cortex, cerebellum, pons and medulla showed no definite changes. The peripheral nerves were normal. No degenerative changes were discovered in the white columns in sections stained after the method of Weigert-Pal.

### **SUMMARY**

Briefly the pathological changes in poliomyelitis are those of a round cell infiltration of the leptomeninges, spinal cord, brain and cerebellum, remarkable peri-vascular round cell infiltration of the blood vessels of the spinal cord and oblongata, particularly those distributed in the ventral gray columns, central gray and adjoining white matter, and much less marked about the vessels of the leptomeninges of the brain, gray and white matter, and least so of the cerebellum. Marked edema, especially in the gray matter of the cord and medulla with distinct

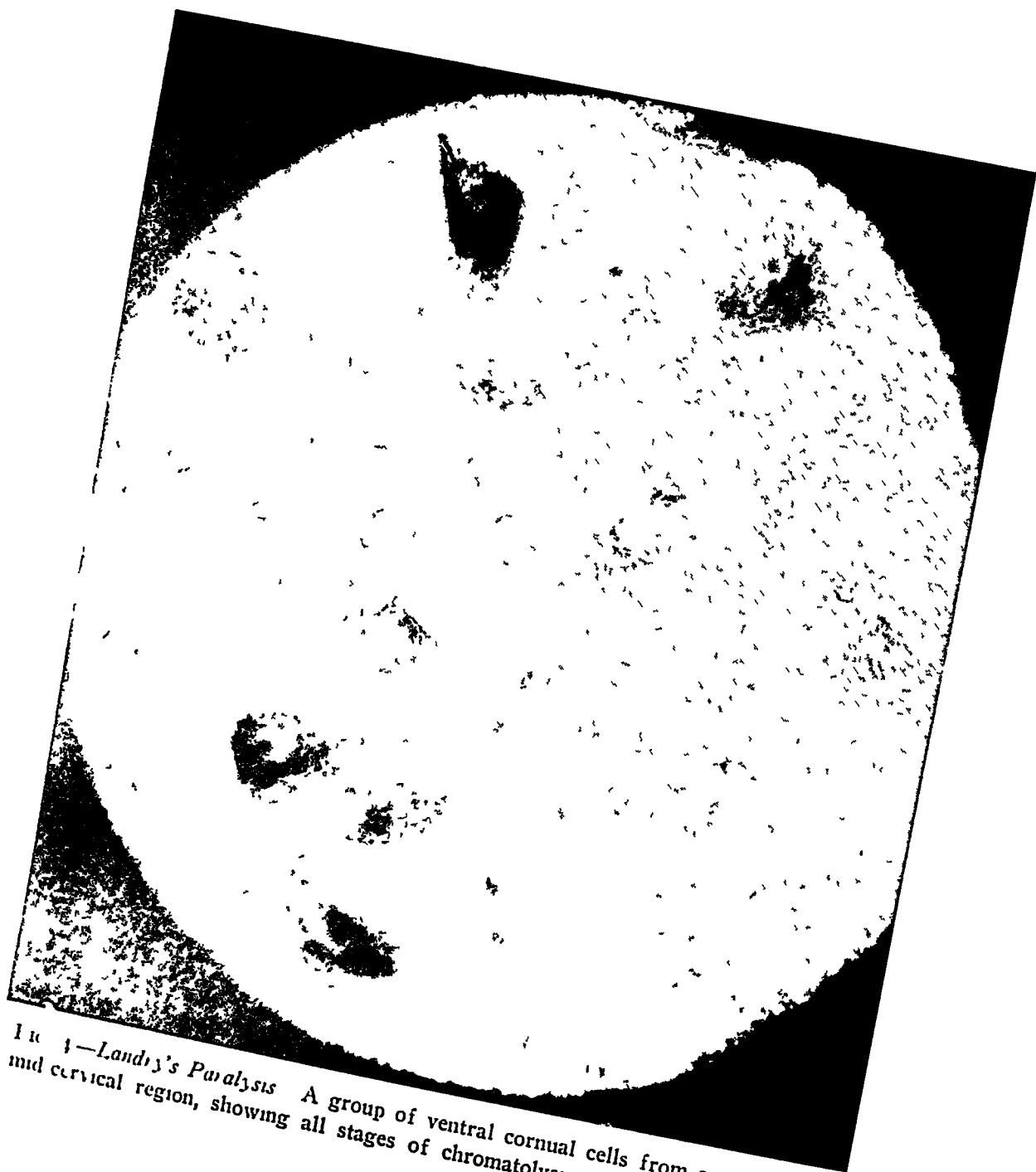


FIG. 4—*Landry's Paralysis*. A group of ventral cornual cells from a section through the mid cervical region, showing all stages of chromatolysis.



nutritional changes or absolute destruction of many of the motor cells therein contained. Both pericellular and perineural round cell infiltrations are quite marked. In other words, the process seems to be a very acute rapidly progressive inflammatory reaction manifested by lymphocytic infiltration of the perivascular, pericellular and perineural lymph spaces, due to the specific virus of the disease.

\*The pathologic changes in Landry's paralysis, on the other hand show but slight or no round celled infiltration, no definite pericellular, perineural or perivascular infiltration. If one compares side by side sections of various levels of the spinal cord of poliomyelitis and Landry's paralysis, one is struck by the paucity of round celled infiltration in the latter disease.

\*The very active virus or toxin produces degenerative changes involving the whole peripheral motor neurons with especial predilection for their cells of origin in the ventral gray columns of the spinal cord, and motor cranial nerve nuclei of the oblongata. These

changes result in chromatolysis, displacement of the nuclei, neuronophagia, many shadow cells, or the complete destruction or effacement of the cells. Small hemorrhages are not at all uncommon, many thrombosed vessels are to be found. The peripheral nerves in many cases also show definite changes. The process seems to be a rapid degenerative type, rather than inflammatory in character.

#### CONCLUSIONS

1 I wish to lay especial emphasis on the absence in this case and two others studied, together with many of the recorded cases of the Landry symptom complex in the literature, of mononuclear round cell infiltration of the pia, vascular walls and gray matter, which is so characteristic pathologically of poliomyelitis.

2 These cases cannot be relegated either on clinical or pathologic evidence to the adult type of poliomyelitis or multiple neuritis.

3 The symptom complex known as Landry's Paralysis seems to be due to some as yet unknown infectious process which has a special predilection for the peripheral motor neurons.

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\*Pathology of the Nervous System by Buzzard and Greenfield, page 211

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# Agranulocytosis: Report of Five Cases with Two Recoveries.

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**D**URING the past few years a considerable literature has accumulated dealing with agranulocytic angina or agranulocytosis. This consists of case reports, autopsy studies and discussions as to the nature of the condition. Several explanations have been offered, no one of which is entirely satisfactory. That it is a clinical entity as thought by Schultz<sup>1</sup> and others is seriously questioned, many observers taking the view that it represents merely an unusual response of the leucocytes to infection as was held by Turk,<sup>2</sup> who described an identical picture under the title of "Septic diseases with destruction of granulocytes."

Of the cases reported, the constant and characteristic feature is the blood picture. There is a striking leucopenia, the total count going as low as 100 cells per cubic millimeter, of which less than 10% are polymorphonuclear cells and more than 90% lymphocytes. The red cells and hemoglobin show little or no variation from normal, the platelets are normal. In most cases ulcerative or necrotic lesions have been observed in the mouth or throat and occasionally elsewhere on mucous or cutaneous surfaces. In many instances these have appeared after the disease was well under way. High fever of a

continuous type, chills and prostration are the rule, while in about half the cases jaundice has been noted. The onset is usually abrupt and the disease progresses to a fatal termination in one or two weeks, most of the patients developing broncho-pneumonia. Recovery has been rare. Autopsy studies have disclosed no characteristic findings either in the bone marrow or other tissues.

Of five cases with agranulocytic leucopenia observed by the writer, three died and two recovered. The three fatal cases conform in most respects to the now well-known picture of agranulocytic angina and are described briefly. The two that recovered are reported in more detail, inasmuch as recovery from this condition is comparatively rare and several features in the course of the disease are of interest in connection with the general question of agranulocytosis.

## CASE REPORTS

*Case 1* Married woman, 52 years of age, seen at the Memorial Hospital in consultation with Dr C C Coleman. Her past history was entirely negative. Four days previously she had become suddenly ill with fever, chills and sore throat and had grown rapidly worse. An indurated swelling had appeared on the right side of the neck, incision of which showed only bloody serum.

Examination showed extensive ulceration

of the throat and soft palate which were more or less covered with a dirty white membrane, while in the lungs were signs of broncho-pneumonia. Smear and culture from throat were negative for Klebs Loeffler bacilli, and blood cultures were negative. Leucocyte count was 600 cells per cu m, no polys seen. Death two days later. No autopsy.

*Case II* Single woman, age 40, seen with Drs Anderson and Royster at Westbrook Sanitarium, where she had been under treatment for three months as a mental patient. Her illness had begun five days previously with a sore throat and high fever. At first the throat was diffusely red with one small whitish spot on the tonsil. Later there was ulceration and swelling that ruptured with the discharge of bloody pus.

Examination showed temperature 104, pulse 150, and signs of consolidation in the left lung base. The average of seven leucocyte counts was 250 cells per cu m, no polys were found. Smears from the throat showed a long and short chained streptococcus. Blood culture was negative. The patient died the following night. No autopsy.

*Case III* A farmer of 47 was seen at the office, having been referred by Dr Ferry of Miller's Tavern, Va. He complained of weakness, which came on with an attack of sore throat and grip six weeks previously, and pain in the rectum of two weeks duration. During the attack of grip he was said to be jaundiced. There had been slight diarrhoea but no bleeding.

Physical examination was negative except for extreme pallor with a yellowish tinge, a spleen that extended several inches below the costal border and an ulcer just inside the anus. The blood count revealed a hemoglobin of 39%, red cells 2,160,000, one normoblast seen, leucocytes 1,600, pmn 16%, lymphs 84%. No cord changes were made out, the gastric contents after a test meal contained free HCL and there was no fever. He went to his home, promising to return for further study. Four days later he was

admitted to the Johnston-Willis hospital complaining of pain in the left chest and fever which followed a chill. Examination showed temperature 103, signs of diffuse broncho-pneumonia and some extension of the rectal ulceration. On admission the leucocytes were 1,100 with pmn 14% and lymphs 86%. The patient grew steadily worse and died a week later. The white cells diminished and on the day before death were 200 with 12% pmn and 88% lymphs.

Autopsy showed extensive bilateral broncho-pneumonia. The note on the spleen by Dr W A Shepherd was as follows:

"Spleen measures 15x20 cm. Section shows marked pigmentation and rarefaction of adenoid cells so that the splenic reticulum is visible, in considerable areas, free from cells. Splenic nodules are imperfectly preserved, showing a pronounced narrowing of the areas of condensation around the arterioles. Endothelioid cells are occasionally encountered. In the rarefied areas many distorted cells are seen."

*Case IV* A married woman of 66 was seen at her home in Petersburg, Va, with Dr J D Osborne, her family physician. She had been troubled for two months with pains over the entire body, chiefly in the muscles, and a diseased tooth had been extracted. The gums healed and at no time was there sore mouth or sore throat. For four days she had had fever which began abruptly, going as high as 104 and this was accompanied by diarrhoea, little or no abdominal pain, no blood, slight nausea and occasional vomiting.

The temperature was 103.2 pulse 120, respiration 34. The throat was somewhat red but no ulceration or exudation seen. Over the lower left back a few moist râles appeared but there was no accompanying change in the breath sounds or percussion note. Blood examinations: Hb 68%, rbc 3,200,000, wbc 600, pmn 4%, lymphs 96%. Little hope was held out for recovery, but, on the day following, the temperature suddenly dropped, the patient appeared much better and there was a prompt rise in the leucocyte count with a steady return to normal. Dr Osborne kindly furnished me

with his observations on the course of the fever and blood changes and these are shown in Fig 1

*Case V* A physician of 48 had been examined from time to time over a period of 8 years. He had a slight hypertrophic arthritis, a few apical abscesses for which extraction was done, and several mild attacks of appendicitis with appendectomy and the removal of an appendix described as subacute. Numerous blood examinations had shown nothing abnormal. On March 27, 1929, he was admitted to the Johnston Willis Hospital acutely ill. He stated that ten days previously he had a rather acute pain in the upper abdomen relieved by vomiting. Though not feeling well, he continued to work until two days before admission when the pain again became severe and was accompanied by nausea and vomiting, a temperature of 102 and slight jaundice. The following day his temperature was 104, pain and vomiting continued and some surgical lesion in the abdomen was suspected. For 24 hours the throat had been extremely sore.

The temperature on admission was 103, pulse 90. The throat was deep red, but no ulceration seen, the cervical glands somewhat enlarged and quite tender. The abdomen was distended and generally tender but not definitely rigid. Blood examination showed Hb 75%, rbs 3,820,000, wbs 2,100, pmn 1%, lymphs 99%, platelets 290,000. Cultures of blood and stools were negative. Cultures from throat showed streptococcus. For several days no improvement was noted, pain in throat and abdomen continued with nausea and occasional vomiting, and on March 30th, the leucocytes were 1100 with polys 35%, lymphs 97%. At this time X-ray treatment was arranged to be done the following morning, but during the night the temperature fell and, as the leucocytes showed an immediate rise, no treatment was given. Improvement thereafter was rapid, the course of the temperature and leucocyte count being shown in Fig 2. Subsequent blood counts were of interest, though the patient was free from pain and fever and rapidly gaining strength. There

was a steady rise in the total count with an increase in both granular cells and lymphocytes. On April 4th there were 16,400 leucocytes with polys 53% and lymphs 47%. Following this there was a decline which was gradual and on April 30th a count of 2,850, polys 48%, lymphs 52%, was recorded. A second gradual rise then began and on June 10th the total leucocyte count was 7,800, polys 58%, small lymphocytes 37%, large lymphocytes 3%, eosinophiles 2%, Hb 89%, rbc 4,320,000\*.

#### COMMENT

If the diagnostic criteria laid down by Schultz were strictly adhered to, only two of the cases here presented could properly be included under the term agranulocytic angina for the reason that no necrotic or ulcerative throat lesions were demonstrable and two cases recovered. There is no agreement, however, among writers on the subject that the throat lesions are an essential part of the picture or that they bear any etiologic relation to the fever and blood reaction. The fact

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\**Subsequent Note on Case V* Except for slight nervousness and occasional insomnia he was free from symptoms and blood was normal up to June 24th. On this date he became ill rather suddenly with sore throat, general aching and fever. He was admitted to the hospital and, when seen about 12 hours after the onset, the throat was red, the cervical glands enlarged and tender and there were several elevated, dusky red, tender nodules about 1 cm in diameter over each cheek and a similar nodule on the buttock. Leucocytes 1500. Small lymphocytes 100%. Fever was high and continuous, a grayish membrane appeared on the fauces, followed by extensive ulceration. Daily count of leucocytes showed only small lymphocytes, the total number going as low as 200. X-ray treatment was given without apparent effect. Death occurred July 2, 1929.

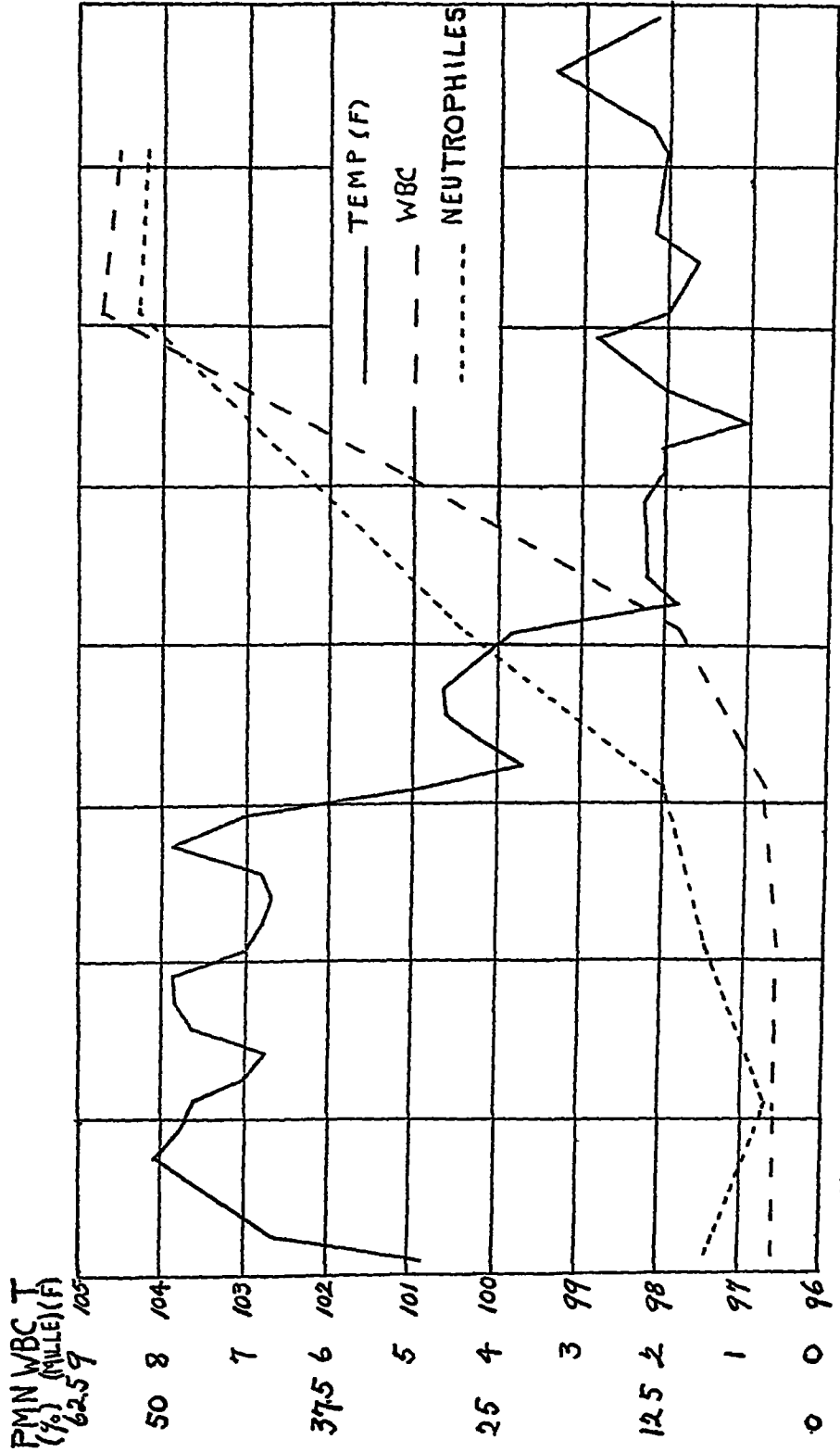


FIG 1 Coincidental rise in total and neutrophile count following fall of temperature in Case IV

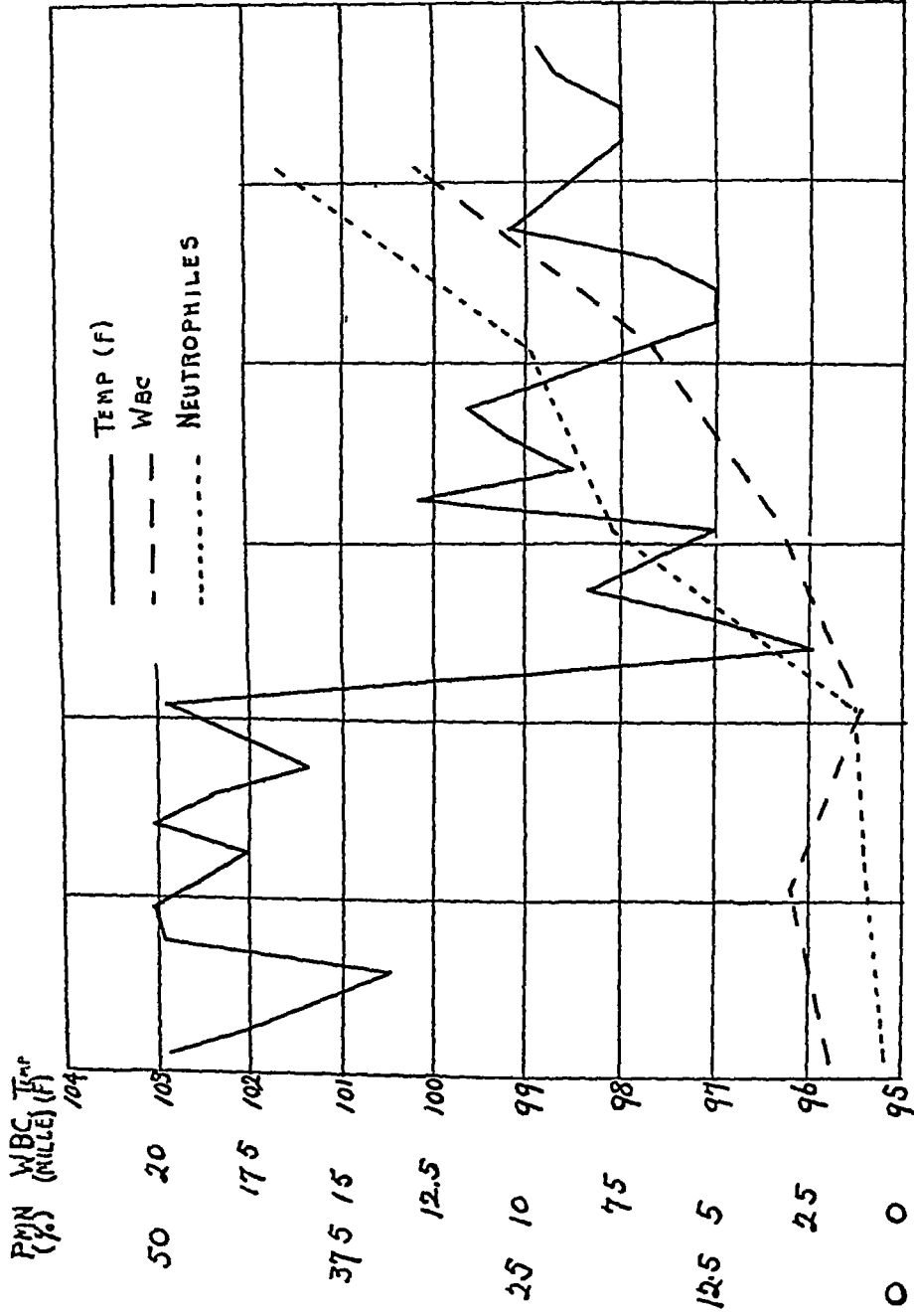


Fig 2 Crisis-like fall in temperature in Case V accompanied by sharp rise in total leucocytes and neutrophils



that they often appear after fever and blood changes are well established would indicate that they are secondary, and this view is held by a number of observers. In Case III enlarged spleen, secondary anemia, agranulocytic leucopenia and rectal ulceration were observed before the onset of fever. There was a history of an acute illness with fever and jaundice six weeks previously, but no blood examination was made at this time. It seems likely that temporary improvement had taken place with relapse later and death.

In Case V of this series there was rather severe sore throat beginning several days after the onset of illness and, though no ulceration was seen, it is readily conceivable that ulceration and necrosis might have appeared, had recovery been postponed a few days longer.

Of forty-three cases collected by Kastlin,<sup>3</sup> only three recovered, and Hueper<sup>4</sup> in a later review of the literature could find only six. One is impressed in reading the case reports available with the energetic treatment

employed, especially blood transfusion. In view of the comparatively normal red cells and hemoglobin, transfusion seems hardly indicated and experience with it so far recorded indicates that at least it does no good. X-ray, given in small doses to the long bones, has received some attention and in a few cases has seemed helpful. In Case V, X-ray treatment was decided on in the evening and, had it been given at once, instead of delaying until the next morning, an apparently excellent result would undoubtedly have appeared.

The most striking feature of the two cases that recovered is the prompt rise in leucocytes, chiefly in granular cells, which occurred with the crisis-like fall in temperature.

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# Newer Methods in Tuberculosis Therapy\*†

By BENJAMIN GOLDBERG, M D , *Chicago, Illinois*

**A**T the International Congress on Tuberculosis in Washington in 1908, in greeting the delegates, Dr Edward Livingston Trudeau, said "For thirty-five years I have lived in the midst of a perpetual epidemic, struggling with tuberculosis, both within and without the walls, and no one can appreciate better than I do the great meaning of such a meeting I have lived through many of the long and dark years of ignorance, hopelessness, and apathy, when tuberculosis levied its pitiless toll on human life unheeded and unhindered, when, as Jaccoud has tersely put it, 'The treatment of tuberculosis was but a meditation on death' But," Trudeau continued, "I have also lived to see the dawn of the new knowledge"

Trudeau was, indeed, present at the dawn, it is unfortunate that this great pioneer died before he had opportunity to witness the further realization of that dawn If Trudeau lived today, the measure of his gratification would be more complete He would sense in the present day tendency of our tuberculosis program, a stronger tone of

optimism, he would feel, we think, that his dream was well on the road to fulfillment, that present tendencies and present measures of prevention and therapy were, at length, to master tuberculosis

In the decade and a half since Trudeau died, many features have been added to the tuberculosis program which tend to accelerate the progress and intensify the activities of the anti-tuberculosis campaign The broad foundations laid by Trudeau and other early workers have been sufficiently strong and stable to support the superstructure of the more recent scientific contributions These later contributions, unfortunately, are not given the widespread attention that this major disease, which interests us, demands

*Prevention* We will first consider prevention Both from the point of view of its chronological sequence and from the point of view of its importance, the subject of prevention demands first place in our consideration

## IMMUNIZATION

The subject of artificial immunization of the human host is today receiving special attention Calmette, of Pasteur Institute, and his co-workers have focused our attention on a method of immunity developed by them According to the Calmette method, an

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attenuated culture of bovine tubercle bacilli, attenuated through repeated growth on bile potato media, is used for inoculation

The *Bacillus Calmette Guérin* (B C G) is administered orally during the first ten days of life, the approximate period, according to von Behring, during which the intestinal mucosa is permeable to the bacillus tuberculosis. Calmette claims for the culture of bacilli, chosen and grown according to his formula, that it is absolutely avirulent and produces an immunity to tuberculosis within a period of approximately four weeks. This immunity, it is claimed, is sufficient to protect the child against even the intimate contact represented by exposure of an infant to a mother suffering with open tuberculosis.

The *Bacillus Calmette Guérin* has been in use, experimentally, for a period of years, and to date, perhaps, more than two hundred thousand infants have received protective inoculation. Unfortunately, the statistics compiled concerning the tuberculosis morbidity and mortality among inoculated children are not above criticism. Sufficiently exhaustive investigation of the individual case has apparently not been carried out, and routine post mortem examination has not excluded tuberculosis. This fact, combined with the observation that other workers in attempting animal passage with the *Bacillus Calmette Guérin* organism, have, in certain instances seen death occur. Death, accompanied by asthenic emaciation and enteritis has occurred in the guinea pig, and in other instances, post mortem has revealed a definite tuberculosis.

The question of allergy in connection with artificial immunization is of interest, but rests for the present on debatable ground. Certain questions are still unanswered. Does such allergy, as is indicated by the presence of a positive tuberculin reaction, constitute an immunity? Is the absence of a positive tuberculin reaction indicative of lack of immunity? Is it possible, as Calmette claims, that in certain instances immunity may be present in the absence of a positive tuberculin reaction?

We cannot answer these questions today with any approach to scientific finality. I feel, however, that we should not be too hasty to condemn, if immunity to tuberculosis can be produced by this method, or a similar method, the entire tuberculosis problem is on the verge of solution.

We have done some work along the lines of inoculation in the Municipal Tuberculosis Sanitarium. After a year or more, however, of animal experimentation in our laboratories, it was deemed not advisable to attempt human inoculation. As the matter was still debatable, it was considered better to defer human immunization until such time as the results of years of work abroad should prove conclusive.

*Contact Exposure* If we consider tuberculosis from the viewpoint of hygiene alone, we are confronted by the problem of a germ-borne or infectious disease, which is practically ubiquitous. The disease is preventable, we know it is preventable. If we can prevent infection from entering the body of its human host, it goes without saying that no pathologic process and no disease can result. The difficulty, of

course, in the way of prevention, is that, as stated, in city life at least, the bacillus is practically ubiquitous. The infection is so far reaching and the manner of infection so varied, that sooner or later a majority of city dwellers develop a positive tuberculin reaction.

We now come to the difference between infection and disease. Although the organism, as stated, is practically ubiquitous, and although infection in city dwellers is the rule rather than the exception, the proportion of the general population that succumbs to tuberculosis is relatively small.

Why is it that infection is not more frequently followed by disease? What is the pathogenesis of tuberculosis in the adult human host? Does the disease result as an endogenous reinfection from the primary focus, or, on the other hand, does active disease supervene as an expression of exogenous superinfection? What is the relation of resistance to infection? In what way is resistance in its turn bound up with such considerations as the amount or degree of infection, the time of life in which infection occurs, race history, etc.?

These and other questions are as yet not solved, nor do they appear easy of solution.

We do know, however, from clinical observation and statistical compilation, that the matter of contact, particularly intimate contact with active, open tuberculosis, is one of the most important and most constant etiologic factors in the production of the disease.

In Chicago, we consider the study and control of the contact as of first

importance. In addition to segregating the children under sixteen years of age from the open case, we have established a new system of contact control. A special chart of distinctive green color, containing special "contact sheets" is used for the individual adult or child who has lived in the same premises with a case of known tuberculosis. The distinctive color of the chart makes it readily recognizable in the files, and renders the compilation of contact statistics much easier.

The system of contact study applies not alone to children. Realizing the importance of contact even in adult life, and realizing, furthermore, the possibility of superinfection, our system of contact study was extended to include observation of *all* contacts, adults as well as children. Every individual, adult or child, who has been exposed to open tuberculosis, is kept under constant surveillance and is re-examined at definite intervals. Advice regarding habits, diet, general health building and disease prevention, is given as part of the program. Close supervision and frequent examination of contacts permit of early diagnosis, and this, of course, is an essential objective in an anti-tuberculosis campaign.

In the two year period, 1927 and 1928, 9,891 new contacts were examined, and 645 cases of tuberculosis uncovered. Of the 645 cases, 545 were cases of pulmonary tuberculosis, 93 were gland tuberculosis, and 7 bone and other forms of tuberculosis.

*Control of the Open Case* The control of the open case is the prime consideration in our present day program of prevention. The civilized

world, both lay and professional, is being aroused to the necessity of segregation. Prevention of infection, particularly in childhood, is essential and without adequate control of the positive sputum case this objective is unattainable. I may perhaps define the situation better if, for a moment, I draw your attention to the situation in Chicago.

In Chicago at the close of 1928, there were 3,167 positive sputum cases under supervision. Of these only 25 were in contact with children, and these 25 were in process of clearance. During the year there were 942 cases in contact. Contact was broken in 917 cases and 1,927 children thus protected from further infection.

The separation of the child contact from the open case of tuberculosis is made possible through a paragraph in the State Rules and Regulations for the Control of Tuberculosis, which reads: "No child under the age of sixteen shall live in the same home, apartment or other place of abode or habitation with any person suffering from active tuberculosis (consumption)." This law is rigidly enforced, irrespective of the social or economic status of the individual, and its enforcement, we are convinced, constitutes the most important phase of our preventive work.

*Chest Surgery* Until recently there was little hope for the advanced, progressive case in which pneumothorax and routine treatment had met with an unfavorable response. The physician, however, schools himself against despair. He is imbued with the underlying significance of Mme Swetchine's saying, "God has

prohibited despair." Ingenuity, optimism and courage have opened up a new avenue of hope for the condemned—the advanced consumptive. Surgery has come to the aid of the phthisiotherapist, who formerly had relied principally upon the time honored triad—rest, fresh air and food.

There are, it is estimated, in this country, approximately a minimum of 500,000 to a maximum of 1,000,000 active cases of pulmonary tuberculosis. Statistics compiled from the larger urban centers indicate that over fifty per cent of individuals with tuberculosis, when they first appear for treatment, are already in an advanced stage of the disease. This is regrettable and constitutes a serious problem, the more advanced the disease process, the less likelihood of recovery. Some of these patients, already beyond the favorable phase of incipency, had in the past, before the advent of chest surgery, only the benefit of artificial pneumothorax. The limitations of pneumothorax, however, are very great and its scope of usefulness comparatively very narrow. Many, or perhaps even the majority of the advanced cases, were either entirely unfit for pneumothorax therapy or were only partially benefited by the procedure.

It was to this group of patients, to patients who could not receive benefit from routine treatment or from pneumothorax, that chest surgery came as a new and un hoped for measure of salvation. It is estimated that there are about 40,000 such individuals in this country, individuals from whom, according to the old routine, the prognosis was very grave, but for whom,

owing to the introduction of thoracoplasty, hope is kindled anew

In recent months, as our knowledge concerning the value of the surgical procedures has become more clearly defined, it has become evident that the field of chest surgery holds much greater possibilities than was at first supposed. It is not only to the far advanced, hopeless individual that chest surgery offers a measure of hope. In the early case, also, as is becoming more apparent each day, chest surgery has a pronounced sphere of usefulness. A simple surgical procedure, applied without pain or danger, may result in more improvement to the early case than weeks or even months of sanatorium stay.

One such procedure—the crushing or removal of the phrenic nerve, we mention briefly. The chief value of this procedure lies in the fact that it produces an almost absolute relaxation of the lung on the side operated upon. This relaxation of the lung allows a practically complete pulmonary rest and has the additional benefit of compression from the relaxed elevated diaphragm.

The phrenic nerve is easily exposed, injected, crushed or removed with a technic which must be carefully carried out, but which may be easily learned. If one merely visualizes the immobilization of the lung achieved by this method, one can readily understand why the healing of an early tuberculous process may be promoted under this plan better and more rapidly than through the method of any procedure formerly used. Our experience indicates that it will supplant pneumothorax in about 80 per cent of

cases where previously the latter had been indicated.

The other surgical procedures are extrapleural pneumolysis and thoracoplasty. In the few years it has been our privilege to utilize them, we have learned that these operations are specific procedures, each one with its own indications and contra-indications, its limitations and its possibilities.

There are three guiding principles which are absolutely essential to the success of chest surgery. In the first place, it is necessary that the surgeon have the requisite skill and experience for this type of work. In the second place, it is essential that the cases chosen for operation be suitable. In the third place, it is necessary that the institution which does chest surgery possess all the equipment of a well-ordered, general hospital, and be in position to give the same pre- and post-operative care as is characteristic of such a hospital.

It may not be amiss to mention in passing, that apart from chest surgery the sanatorium based on the general hospital plan, is in a position to give efficient and timely treatment to the surgical complications of tuberculosis. A tuberculous patient suffering with a non-tuberculous complication, as Graves' disease, is struggling along under double handicap. In the case of Graves' disease, for instance, the removal of the sources of toxemia by means of operation will greatly aid the patient in his battle against tuberculosis.

*Diet* Studies and chemical research inaugurated within the last few years, are opening up a new vista to general medicine, and in particular to phthisiotherapy. We are beginning to realize

that body chemistry can best be influenced through the medium of food. The importance of the mineral balance, both in health and in disease, and the relation between this mineral balance and the dietary, has not, in the past, been sufficiently appreciated. An adequate mineral supply is especially indicated in tuberculosis. Available evidence seems to show that the loss of mineral salts is higher in tuberculous patients than in the normal individual. The output of chloride is generally increased.

From Germany there comes to us statements concerning new dietetic principles which, according to those making the experiments, seem to be unusually efficacious in aiding the recovery of tuberculous individuals. Gerson and Sauerbruch stress the importance of the mineral balance and emphasize the advantage of salt restriction. The salt restriction is advised even in the face of an increased chloride output, because it is claimed that salt increases cell metabolism which of itself tends to be excessive in tuberculosis.

In the Gerson diet such articles of food as common salt, smoked and pickled meats, ham, sausage, conserves, smoked or salted fish, bouillon cubes and vinegar are prohibited. Fresh meat, internal organs such as brain, liver and kidneys, fresh fish, sweetbreads, Liebig's extract, beer and wine are allowed in moderation. Cocoa, coffee and tea are allowed in amounts sufficient only to color milk. Foods advised to be taken in large quantities are milk, fruits of all kinds, salads, vegetables, and salt-free butter. Phosphorized cod liver oil and certain mineral preparations are advised in addi-

tion to the diet. The mineral compounds advised contain calcium, magnesium, strontium, sodium, bismuth and aluminum as cations and, as anions, phosphate, sulphate, thiosulphate, silicic acid, carbonate, bromide, salicylate and lactate. A definite attempt is made to keep down the intake of sodium chloride and increase the intake of the other minerals.

In addition to the minerals, the vitamins, of course, are of importance, and their importance in recent years has been greatly stressed. Vitamin additions were made to the ordinary diet in the treatment of tuberculous enteritis by Dr. Mack McConkey, of the New York State Hospital, at Raybrook, New York, and marked benefit apparently resulted from the use of these substances.

In the research department of the City of Chicago Municipal Tuberculosis Sanitarium, for the past several years, there has been intensive study on the influence of diet in animal tuberculosis. It has been established only in the last two years that adequate vitamins and minerals in definitely proportioned amounts determine the question of susceptibility or resistance to disease.

On certain deficiency diets animals have become prone to tuberculosis, have developed the disease, and have had the tuberculosis healed when the diet formula was changed to one which was adequate.

Insofar as animal experimentation is concerned, the solution of the diet problem seems almost complete. Our next step was to carry the lesson learned in the laboratories to the bedside. In the past few months we have been modifying and applying the les-

sons gained from animal experimentation to groups of tuberculous individuals. We hope before many months have elapsed that we will have something concrete to offer along this line.

We believe that results already obtained indicate that a diet plan along scientific lines will be, perhaps, the most important factor in the cure of tuberculosis. New discoveries are in the offing, which seem to confirm this opinion. The teaching that the basic protein, carbohydrate and fat constituents are of importance will be confirmed. In addition, the vitamin and mineral quotients, in their proper balance, given in a diet arranged according to the new formula will be determined as the most important factor in the healing of the tuberculous process. Furthermore, we believe that diet on these principles will prove to be the greatest influence in building up resistance to tubercle growth and in preventing development of the disease in pretuberculous and contact cases.

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To summarize, then, today we are instituting more effective measures of prevention. We must, first of all, attempt, insofar as possible, to prevent disease by minimizing infection particularly in childhood, and with this thought in mind exercise a conscientious and continuous supervision of the open case. We knew from experience that exposure to the open case is the most constant etiologic factor in phthisiogenesis. We must, consequently, do everything in our power to prevent undue prolonged or intimate exposure, particularly in childhood. While exogenous superinfection in adult life can not be ruled out, the weight of evidence still points to the

endogenous reinfection of an old focus as the usual mode of phthisiogenesis.

When exposure has occurred, the contact must be studied and observed over a long period of time, or even indefinitely. Prevention on the basis of artificial immunization does not, as yet, rest on a scientific basis. The possibilities of artificial immunization, however, are so tremendous, if the procedure should ever prove successful, that we can not afford to indulge in destructive criticism.

The tendency today is to supplement the routine procedures of yesterday with the new surgical procedures—crushing of the phrenic nerve, phrenico-exeresis, extrapleural pneumolysis, and thoracoplasty. Even in the matter of the early case, the new procedures have a scope of usefulness and the potentialities of this field are being more fully realized day after day.

The tendency, today, finally, is to emphasize the importance of diet, both in the treatment of tuberculosis and in the field of tuberculosis prevention. New work both in Germany and the United States indicates that the minerals and vitamins, in their proper ratios, are essential for the healing of the tuberculous lesion.

On the whole, the tendency, as may be erroneously supposed from this paper, is not *away* from the time honored triad—rest, fresh air and food. This triad still forms, as it were, the heart of the therapy problem and must remain. We are, however, today not content with the therapeutic potentialities of the triad *per se*, the tendency is to supplement the therapeutic value of rest, fresh air and food with the newer measures which science and surgery have placed at our disposal.



# Ophthalmoplegia and Graves' Disease\*

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IF one may judge from the literature ophthalmoplegia as a sign of Graves' disease is extremely rare. Yet other eye signs as exophthalmos, lack of coordination between the movements of the upper lid and the elevation or depression of the visual axis and many others are well recognized and constitute some of the cardinal signs of exophthalmic goiter. Heuer (1) in 1916 reviewed the literature of the disturbance in function of the cranial nerves associated with exophthalmic goiter and reported a case of external ophthalmoplegia with Graves' disease. He pointed out how infrequently it occurred but that the ocular muscles were the most frequently involved of the cranial nerves. He discussed the possible mechanism of the development of the phenomenon but arrived at no definite conclusion. Holloway, Fry and Wentworth (2) recently studied in detail the ocular signs in one hundred unselected cases of goiter and mention that in two cases of goiter they observed paresis of the superior oblique muscles.

Because a complete ophthalmoplegia externa preceded other clinical signs and symptoms of a typical Graves' disease syndrome by months, the following case is reported.

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## CASE REPORT

W S, a Jew, age forty, married and an insurance agent by occupation, was first admitted to the Ophthalmology Out Patient Clinic of the University of Michigan Hospital October 11, 1927. He complained of drooping of the left upper eyelid and diplopia for six months previous. The ptosis at times varied in degree. Fourteen months previous he had what was called rheumatism and some abscessed teeth were removed, also his tonsils. Examination revealed normal pupillary reactions and vision O D 4/30, O S 6/30. There was a slight exophthalmos and suspicion of lid lag with partial paralysis of the external rectus O U and of the muscles supplied by the third cranial nerves, more marked in O S. Convergence was limited. The fundus showed slight perivasculitis. The visual fields were contracted. Other cranial nerves functioned normally. The tendon and skin reflexes were normal and all forms of deep and superficial sensation were present. There was roentgenographic evidence of a left maxillary sinusitis. Skull X-rays were normal, as also those of the chest. Blood and spinal fluid Wassermann tests were negative. The spinal fluid examination was normal in all respects.

On February 23, 1928, the patient reported that for a while the ptosis of the left lid was much improved. His appetite was poor and he felt tired most of the time. He now weighed one hundred twenty-eight pounds and nine months previous his weight was one hundred forty-eight pounds. There was practically a complete bilateral external ophthalmoplegia but otherwise the neurological examination was normal. He was worrying about the possibility of permanent visual disability. He was very nervous, ex-

citable and perspired freely. Insomnia was a prominent feature of his present state. Shortness of breath and palpitation of the heart on slight exertion existed. The thyroid was not enlarged. There was a fine tremor of the extended hands. On March 10, 1928, the basal metabolic rate was plus 48% with a pulse rate of 112. On March 15, 1928, the basal metabolism was plus 41% with a pulse of 100. Weight at this time was one hundred eight pounds.

On April 4, 1928, after a period of lugolization a subtotal thyroidectomy was done. Pathologic examination of the thyroid tissue was an "over iodized exophthalmic goiter."

The immediate post operative period was uneventful. On May 18, 1928, about six weeks post operative, the patient returned for a check up examination. He reported that he felt "one hundred per cent better." The nervousness and insomnia improved. He now weighed one hundred forty-two pounds. The pulse was still around 100. He looked healthy, however, there was little improvement in the condition of his eyes. The basal metabolic rate was plus 7%.

He was last seen February 6, 1929, and reported his general health to be good. The basal metabolism was minus 2% with an average pulse rate of 80. The differential count showed the lymphocytes to be 46%. The ptosis had improved considerably. Exophthalmos was still very marked. There was some improvement in the excursion of the movements of the eyeballs. He was now back at his usual work.

#### COMMENT

At first the etiology of the ophthalmoplegia was somewhat obscure. The usual causes of ophthalmoplegia at this age could be easily ruled out except for possibly myasthenia gravis. Ophthalmoplegia is usually the first manifestation of myasthenia gravis but is soon followed by bulbar palsies. Even after the ophthalmoplegia became almost complete no signs of fur-

ther palsies presented themselves. Coincident with the ophthalmoplegia or shortly after its onset other manifestations such as nervousness, tremor, loss of weight, etc., etc., directed our attention to the possibility of thyrotoxicosis. In support of this presumption additional evidence of a striking rise in the metabolic rate was obtained and the clinical course following thyroidectomy leaves little doubt in the minds of the most critical as to the presence of thyrotoxicosis.

While ophthalmoplegia is almost always said to be present in true cases of myasthenia gravis, one should keep in mind that it is strictly speaking neither a paralysis nor a paresis. It is a peculiar tiring of the muscles after exertion and rapid recovery after rest. In our case, rest did not seem to relieve the functional disability.

Myasthenia is recognized as a common symptom of myasthenia gravis and Graves' disease. In myasthenia gravis the basal metabolism is usually below normal. In two cases of myasthenia gravis recently studied by the author and showing the typical ophthalmoplegia, myasthenia, bulbar weakness and typical electrical reactions, the basal metabolism was in one case on one occasion minus 23% and on another minus 24%, and in the other case minus 9%.

Many observers have noted a typical lymphorrhagic infiltration of the muscles in myasthenia gravis and this has now been accepted by many as pathognomonic of the disease. Dudgeon and Urquhart (3) have recently shown lymphorrhages in the muscles of eight out of nine cases of exophthalmic goiter and they have been most marked in

the ocular muscles. The muscles in proximity to the lymphorrhages may show atrophic changes while an interstitial myositis is by no means uncommon.

Changes in the thymus are common both in myasthenia gravis and exophthalmic goiter. The changes in the thymus in myasthenia gravis vary from normal histologic structure, tumor or a simple hyperplasia. The tumors of the thymus found associated with myasthenia gravis are usually made up of young thymic tissue. Hyperplasia of the thymus in exophthalmic goiter has recently been shown by Potter (4) to exist in all cases.

#### CONCLUSION

Myasthenia gravis and exophthalmic goiter present many clinical and pathological features in common. Both may exhibit extreme myasthenia and ocu-

lar palsies and pathologically show lymphorrhagic infiltration of the muscles and other evidence of thymic-lymphatic constitution. The preponderance of evidence in both conditions points to the likelihood of a tendency to an endocrine dysfunction possibly of congenital thymic origin.

#### SUMMARY

1 A case of exophthalmic goiter with external ophthalmoplegia preceding the other signs and symptoms is recorded.

2 The close relationship between myasthenia gravis and exophthalmic goiter from the clinical and pathological standpoint is noted.

3 The essential difference in the clinical picture between exophthalmic goiter with ophthalmoplegia and myasthenia gravis is the difference in the basal metabolic rate.

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# Hemorrhagic Nephritis\*

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IT seems desirable to present to you briefly the subject of hemorrhagic nephritis for several reasons -

(1) Although the disease is fast being recognized as a definite entity, there is still but little in the literature to indicate such recognition

(2) Undoubtedly many cases are prematurely discharged as cured Knowledge of the disease and more careful and accurate urinalyses should indicate that the renal lesions persist and that treatment must be continued to avoid a chronic nephritis and death

(3) Fairly often these cases fall into the hands of the G U surgeon because of the hematuria All too frequently they are subjected to a distressing cystoscopy which could be avoided by a knowledge of the disease and careful microscopic urinalyses

The object of this talk is to give you a summary of the facts that we have observed during the last few years at the Brigham Hospital

That the incidence of hemorrhagic nephritis is not great is indicated by the fact that out of a total of 1593

cases of nephritis of all types seen in the first 15 years of this hospital only 36 were diagnosed as "hemorrhagic" We are sure, however, that with the more common recognition of this disease as a separate entity more will be found

The data to be referred to in the rest of this paper are based on a study of the last 23 cases A previous paper by O'Hare and Walker\* described observations on 18 cases seen in our wards previous to 1923 Five of the earlier cases are included in this series

Information concerning the etiology of this disease may be gathered from a glance at Table 1

This indicates that by far the commonest cause of the disease is an upper respiratory infection Often this was so mild that little attention was paid to it at the time Frequently, too, we believe that the initial attack of the nephritis is so mild that it fails to be recognized and much valuable time is lost Closer observation suggests that most of the antecedent infections are those attributed usually to the streptococcus This possible relationship seems to be borne out by skin tests done by Dr Derrick Seven of our cases have been tested thus far and every one of them indicates a sen-

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\*From the Medical Clinic of the Peter Bent Brigham Hospital Read at a meeting of the American College of Physicians, April 8-12 1929

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\*Atlantic Medical Journal, 1923

TABLE I

## Etiology

Upper Respiratory Infections (Tonsillitis, colds, "grippe", etc )	12
Rheumatic Fever	3
Scarlet Fever	3
Unknown	3
Intestinal Obstruction	1
Osteomyelitis	1
	—
	23

sitivity to these organisms. Five are sensitive to hemolytic streptococcus and two to the viridans strain. By contrast, skin tests done on other types of nephritis thus far indicate that the majority are non-sensitive.

A few words concerning the pathology of the disease are in order. The disease in the acute stages is so rarely fatal that almost no pathological observations are available. When it has been possible to observe the pathology, it has proved to be a subacute and chronic glomerular nephritis. The more acute lesions are represented by thromboses of afferent glomerular vessels, hyalinization of capillary walls, and rupture of these with hemorrhage into the capsule or into the tuft itself forming a lake of blood. All stages of glomerular injury from these lesions to complete obliteration may usually be seen in the same slide. The subtended tubules atrophy, but no very active degeneration is observed. The marked variability in the degree of glomerular injury suggests that the persistence of the microscopic hematuria is due to the progressive injury to one glomerulus after another.

Clinically the disease starts much like any acute nephritis following an infection. Edema is as a rule relatively mild. Although one cannot always

make the proper diagnosis with certainty in the early stages, one can suspect it by the great predominance of red cells in the urinary sediment. In a comparatively few days the edema disappears and the ratio between red cells and white cells or small round cells seems to increase, though a count of the total number of red cells might actually show a decrease. In the course of a period varying from several days to a few weeks the cellular and granular casts materially lessen, the white blood cells and the renal epithelial cells practically disappear, leaving a sediment consisting almost entirely of erythrocytes and a few hyaline or red blood cell casts. In the meantime, the amount of albumin has fallen from a trace to a very slight trace or even less. This is the dangerous period because while some clear up entirely in a short time, many are discharged at this point because the doctor pays too little attention to the small amount of albumin and the slight microscopic bleeding. The common story is for the patient to continue to bleed in small amounts with a sharp flare-up following each cold or other infection until eventually the function of the kidney falls, the blood pressure rises and uremia and death occur. Occasionally hemorrhagic nephritis changes to or

becomes complicated with another type of nephritis Three of our group originally diagnosed hemorrhagic nephritis are now fairly typical nephrosis patients

One might think that with the more or less continuous bleeding anemia would be marked This is, how-

ever, not the case For a long time the bone marrow seems able to take care of the slight but continuous blood loss Eventually a mild secondary anemia occurs The figures for 14 cases in which special attention was given to the blood findings are indicated in Table II

TABLE II

	<i>No of Cases</i>	<i>Findings</i>
Blood Calcium	6	Normal
Clotting Time	14	7 prolonged
Bleeding Time	14	1 prolonged
Platelets	14	8 decreased (mod sodium citrate method)
Fibrinogen	12	0 low, 9 high, 3 normal
Rbc	14	Av 3,500,000
Hbg	14	Av 70-75 per cent

This table indicates that there is no consistent lack of any elements dealing with coagulation of the blood although the clotting time was somewhat prolonged in about one half of our cases and the platelet count was

decreased in more than one half The fibrinogen was actually increased in most of our group We know of no reason for this last

The prognosis is indicated by Table III

TABLE III

No of cases	23
Dead	2
Living	21
Recovered completely	10
Chronic Hemorrhagic Nephritis	8
Nephrosis	3

This table suggests that slightly less than one half of these patients recover. The two patients that died lived about six years from the time the lesion was first diagnosed On the other hand, we know at least one patient that is still alive eight years after the onset of the disease and when last seen two years ago showed persistent hematuria.

As far as the differential diagnosis is concerned, it should be said that in

the most acute stage no certain diagnosis may be possible The diagnosis may be suspected, however, from the abundance of blood and the slight edema After the subacute stage is reached, however, there should be no difficulty in differentiating this disorder from anything else by any one who understands the history of the disease and who can and does make careful microscopic urinalyses Whenever one finds a urinary sediment containing red

blood cells varying in number from 4 or 5 per h p f to 200 per h p f, with only a rare white blood cell, prolonged search should be made for red cell, hyaline or fine brown granular casts. The finding of even a few of these especially the first, practically clinches the diagnosis. Of course, it is possible to find casts in an elderly individual who has bleeding from a stone, papilloma, prostatic disease, etc. However, it is extremely rare for such a patient not to indicate the source of his bleeding in other ways. We feel very strongly that many patients could avoid a painful cystoscopy if more intelligent study was made of the patient as a whole and especially of his urinary sediment.

The treatment of this disease is but little different from that of the ordinary acute or chronic nephritic patient, except perhaps in one particular. The patient should be kept at rest in bed until all red cells have disappeared, even if it means months of this treatment. His only chance for a complete recovery seems to be to bring about a complete cessation of bleeding before a chronic lesion develops. Not until one has kept his patient in bed several months and has thoroughly convinced

himself that the hematuria is not going to cease should he give up and allow the patient up and about. The only other item worthy of emphasis is that these patients should not receive an unduly low protein ration. Such a dietetic error might be responsible for increasing the anemia and, possibly, thereby increasing the tendency to bleed. When there is no nitrogen retention and no very acute lesion the patient should receive a salt poor diet containing 1 gram of protein per kilo body weight. The fluid intake should be 1500-2000 cc in 24 hours.

All foci infection should be diligently sought for and eradicated, especially since the streptococcus seems to play such an important rôle in this disease.

Up to now, no methods aimed directly at stopping the hematuria have been successful in our experience. We have tried calcium, ergot, adrenalin, vaccines, transfusion and even decapsulation without avail.

Our work with the desensitization to the specific streptococcus is too new and too brief to justify any discussion. However, the results obtained thus far are encouraging.

# Arachnidism

## A Report of Five Cases of Spider Poisoning,

By J B ELLIS, M D , *Helena, Ark*

ONLY recently, despite thirty years of general practice, have I had my first experience with spider bite poisoning, and these experiences have come in such rapid succession that I am able to report five cases of markedly uniform character which have come under my observation within a short period of time. So rare are such cases in this section of the country that, in the first instance, spider bite poisoning did not occur to me even as a remote possibility. In that case the venomous arachnid was encountered in the dark and was therefore not seen, but in the second, third and fifth cases the offending spider was caught and positively identified as the *Latrodectus mactans*, probably the only poisonous spider in the United States \*

### HISTORY OF THE LATRODECTUS MACTANS

Investigation yields abundant evidence that the bite of the shiny black *Latrodectus* is attended with severe systemic poisoning. Numerous recorders in European and South American

countries, and even in far-away New Zealand, Australia and Madagascar have reported many cases, even viral epidemics of arachnidism. In the United States it seems to be much more rare, nevertheless, here also it has been established as a clinical entity. During the last century more than a hundred fifty cases of poisonous spider bites have been reported by thirty-three physicians\*, mainly from the southern half of the country and especially from California, some of these cases resulting in death. Numbers of cases perhaps go unrecognized because of the unusual and often obscure cause. Since rather extended inquiry reveals my experience with spider bite poisoning to be unique in Eastern Kansas, possibly also in the Middle South, I make this report in an effort to stress the importance of and to aid in its clinical recognition.

### DESCRIPTION

The Arachnida perpetuate the name of Arachne, a Lydian maiden turned into a spider by Minerva for presuming to compete with her in weaving and embroidery, and the particularly and pernicious species with which we are concerned in these five cases, *Latrodectus mactans*, enjoys numerous popular pseudonyms in addition

\*Reference ARACHNIDISM—A Study in Spider Poisoning, by Emil Bogen, M D, Los Angeles. The Journal of the American Medical Association, Vol LXXXVI, June 19, 1926, pp 1524-56



to its many and more dignified scientific synonyms. The California Indians called it the "po-ko-moo". It was their custom to mash it and rub the points of their arrows in it. This virulent arachnid is shiny and coal-black in appearance, the globose abdomen variously marked on the ventral surface with brilliant spots and stripes of red or yellow or both. The most constant of these markings is a bright red patch, shaped like an hourglass, which gives rise to the name, "hourglass" spider. The abdomen is somewhat larger than the cephalothorax, and it so resembles a black shoe button that "shoe-button" spider is a common appellation. The female is much larger than the male, less brilliantly marked, and is always responsible for the bites. In addition, she adheres to the custom of eating her mate and has thus won the deserved sobriquet of the "black widow". What excellent proof of that oft-repeated assertion that the female of the species is more deadly than the male! The black widow is not infrequently half an inch long, when fully grown, and the spread of the long glossy legs may be as much as two inches.

This noxious spider builds for its home a coarse and irregular dark web, hidden in the seclusion of dimly lighted, undisturbed places. It is not infrequently encountered in outdoor privies, as was the experience in each of the cases under my observation, and there it often weaves its web across the seat of the toilet. It will, however, occasionally take up its abode under stones, and in holes, stumps and bushes, as well as frame buildings.

## CASE REPORTS

*Case I* J H, male, colored, aged 39, farmer, residing 18 miles from Helena, Ark

*Case II* J H, male, white, aged 24, teacher, residing at Barton, Ark

*Case III* W H G, male, white, aged 47, merchant and planter, residing at Barton, Ark

*Case IV* W J, male, white, age 36, farmer, residing two miles west of Barton, Ark

*Case V* J E B, male, white, age 40, farmer, residing two miles south of Barton, Ark

The marked similarity of these five cases admits of one description of all. The patients were all males, four white and one colored, all resided in the same section of Eastern Arkansas, each was bitten on the glans penis while in an outdoor privy, all came under my observation from one and one-half to two hours after being bitten, and all reacted to the poison in like manner.

The first symptom in each case was acute burning pain at the site of the bite. This was followed approximately thirty minutes later by severe backache, headache, cramping, aching pain in the abdomen and legs. Each patient experienced sensations of the entire body, swelling, sensations of heat and cold in the body and legs, profuse perspiration, extreme restlessness, and rapid and difficult breathing.

While all five of these cases were tossing and moaning in an agony of pain when admitted for examination, in no instance was there any swelling in the parts inoculated by the bite. The only evidence of the bite was a small red spot, about the size of the head of an ordinary pin, which cleared up in three or four days. In each case the

abdomen was tense with an extreme board-like rigidity, but no tenderness was noticeable. The reflexes were increased in every instance, the blood pressure slightly above normal, the temperature subnormal and the pulse regular but weak and slow, ranging from 60 to 65. In only one instance was it possible to make blood and urine analyses. Case III, W. H. G., age 47, showed a leukocytosis of 16,800, 80% neutrophils, and the urine showed a trace of albumin and some hyaline and granular casts. In all the cases severe constipation followed, probably due to the large amount of opiates necessary to relieve the acute symptoms.

The clinical course varied little in these cases. Within approximately half an hour after the sharp, stinging bite, the onset of the acute symptoms began, and each patient was certainly very sick for a few hours. During the next twenty-four hours pains like a multiple neuritis of arms and legs developed. The symptoms gradually receded but did not disappear for several days.

#### TREATMENT

Fortunately all five of these cases recovered. The treatment was uniform, consisting of (1) a sedative, (2) a stimulant, and (3) eliminative measures. It was necessary to give each of the first four  $\frac{3}{4}$  gr. of morphine to effect any relief from the acute symptoms, but the fifth patient required only  $\frac{1}{4}$  gr., for he evidently possessed a measure of immunity, due to inoculation from a slight bite received a short time before. The stimulant administered was in each case an ampule of caffeine sodium benzo-

ate. Fluids were given freely and such purgatives employed as were necessary to relieve the severe constipation. No local treatment was administered at the site of the inoculation.

#### UNIQUE FEATURE OF CASE V

Case V is worthy of special consideration in that this patient was twice bitten and reacted less severely to the second bite than the other four did to their initial bites, although this second bite was probably of like intensity with theirs. He reported having been bitten, only slightly, however, two weeks prior to coming under my observation. While this slight bite made him ill, he was able to recuperate from the acute symptoms in two or three hours and did not consult a physician. The symptoms caused by the second and more severe bite two weeks later were identical with those of the other four cases except that they were not as acute and it did not require as much opiate to relieve them. Apparently this unique condition was due to a state of partial immunity conferred by the previous inoculation. The evidence in this particular case points definitely to the conclusion that the primary inoculation, even though slight, established a degree of immunity which caused the second and more severe inoculation, following just two weeks later, to produce comparatively mild symptoms.

#### CONCLUSION

My experience with the five cases here cited is not only indicative of the presence of the *Latrodectus mactans* in this section, since it has been definitely identified, but it also illustrates

that arachnidism presents so striking a clinical entity that, once considered as a possibility, the diagnosis is easily made. The history of Case V points to the conclusion that immune blood offers the most logical and effective specific. A study of fifteen cases of this malady in the Los Angeles General Hospital bears out this conclusion. While Bogen's results were not conclusive, intramuscular injection of

convalescent serum proved sufficiently efficacious, when such treatment was used, to warrant continuation of its use and the keeping of a supply of the serum on hand. Should the poisonous black widow infest this section of Eastern Arkansas, it is my belief that such serum would prove to be of definite therapeutic value, if not, indeed, the ideal remedy for this singularly striking affection.

# Medical Genius and Contemporary Criticism

By WINSTON F HARRISON, M D , C M , *Montreal, Canada*

THE concept "Genius" in medicine is difficult to formulate and to define accurately. That genius is a natural gift, something born within a man, the word itself implies. Some would define it as a spontaneous faculty of the mind which accomplishes remarkable things without apparent effort. Yet the genius that has won the greatest and most enduring success has been joined with tireless industry and painstaking. There is an old saying that genius consists in sufficient patience. For convenience let us think here of the word as designating great men in medical history who, whatever their status may be to the psychologist, nevertheless stand out as having contributed in a definite, if not epoch-making way to the growth of truth.

The history of medicine is, in the main, a recount of the biography of great men. As we read about them we applaud with one accord their great works, their important discoveries. We read volumes of praise of them. We honour them. History is kind to great men, the geniuses, much more kind than their contemporaries were. Posterity would rather preserve the words of honour than the words of condemnation. Unfortunately however, the contemporaries of a man whom history has shown to be a genius viewed him

in a far different light than we do. A man who makes a discovery is rarely understood at the time because he introduces some conception which is contrary to the ingrained belief of people. A genius is always a step ahead of the men of his time. It may be a short stride or a long jump according to the nature of his discovery and the time he lived in. In any case he always stands apart, thinks above his fellows. The farther apart he stands the more he is misunderstood. Two kinds of men there are whose minds work on a different plane from those around them, the genius and the lunatic. It sometimes occurs that the two are confused, and time alone is left to determine what the verdict of the majority will be. Thus Dryden wrote

"Great wits are sure to madness  
near allied

And thin partitions do their bounds  
divide."

This attitude of contemporaries should not have been so evident in the realm of medicine because discoveries in science were and must be always based on experiment and proof. Science does not countenance groundless theory. "He alone discovers who proves", is the dictum. Therefore it is all the more astonishing on the face of things that the genius of science was never understood. But the truth

is that while science accepts proof, contemporary critics are often blind to the very strongest proof. Contemporaries are human and fallible and are therefore bound to certain limitations of mind and prejudices. "There's none so blind as the man who *won't* see"

Of all their prejudices and weakness the greatest is undoubtedly the rigid adherence to authority and tradition. It is characteristic of people that they have heroes and are reluctant to have their ideas overthrown. Their hero may be a genius of past ages, later recognized and worshipped, *e g*, Hippocrates, Galen, Hunter. Their hero may be in the form of a religious belief or an old ingrained tradition. In any case, old *Authority* is always the enemy of Genius. Then too, it may be loyalty to a present authority, a personal partisan spirit. People are often unwilling to accept simple explanations because they appear as an insult to their intelligence, as in the case of Semmelweis and Lister. On the other hand the new idea may be too complex for them, as in Harvey's case. Then too there is always the natural inertia of men's minds. Even though a discovery may point out an opportunity for easier and safer going, the minds of people have a tendency to jog along in their old ruts.

Circumstances, then, of a varying character may determine the reception accorded to great advances in science. A discovery made before the world is ready for it, is far more apt to be neglected than acclaimed. The path of genius is never smooth. Walter Bagehot says that the pain of a new idea

is one of the greatest pains to human nature. The influences which determine the reception of genius may perhaps be thought of under three main headings. First there is the influence of the period and the state of knowledge at the time, secondly the influence of personal elements, tradition, mental inertia, jealousy, and so on, and lastly the influence of circumstance, chance, and local conditions, tricks of fortune. The study of biography can never be at its full interest unless the man is placed in his true perspective. This comprehends a knowledge of his time, his contemporaries, what people thought and did when he lived, the forces which influenced their life as well as his.

It is unfortunate that so often the writings of contemporaries are not available to us. Too often we must be content with the bare cold facts which history has recorded that a man of genius met with praise and honour by his fellows or, too often, was scorned, neglected or even persecuted. Some of the refutations of contemporary critics seem perhaps too ridiculous to be interesting to us, but it must be remembered that these men were products of their own age, and had firmly ingrafted in their minds a *reason* for things. People would rather explain phenomena the way it pleases them. Consequently when someone raises this reason to question it was in many cases considered an insult to their mentality as well as to their honoured traditions. Mysticism, superstition and undue reverence for authority, together with the great tendency to confuse hypothesis with fact have probably been the chief factors

in retarding progress, and through all ages these have stuck like black shadows to the onward march of Truth

Let us consider a few men who have shone as geniuses in medical history. They have been chosen it must be admitted more or less at random from amongst the many luminaries of science, but perhaps they will serve as types to illustrate the point.

It is perhaps fitting to mention Vesalius first because he of all the courageous spirits of the renaissance was the great pioneer in scientific medicine. "He was the commanding figure of the 16th century", says Garrison. The renaissance of course swept over Europe like a great wave. The revival of learning was evident in all branches of thought. In medicine the great reform was initiated by Vesalius for it was he who first realized the necessity of dissection of the human body to determine its structure. But the idea really carried more import than that because, strange as it may seem, the method of experiment was never before considered necessary in the study of medicine. Dissection is experimental anatomy. Not until seventy years later did Harvey bring physiology into medicine on the same basis. So then we may say that Vesalius first wielded the most powerful lever of scientific advance in medicine, the method of experiment. Before Vesalius, dissection was generally looked down upon and indeed considered unnecessary. What anatomy was studied was taken verbatim from the works of Galen, who lived more than thirteen centuries previous. Galen's word was law. It would almost seem that men would sooner disbelieve

their eyes than question the works of Galen. When permission was asked of the Church to dissect human bodies, the authorities answered, "It is not necessary unless Galen has made a mistake, and he has not made a mistake, therefore it is not necessary."

Vesalius revolted. Although a scholar and strictly trained in the opinions of his time, he abandoned all prejudice. He began by doubting all authority and investigating for himself with a mind keen and independent. His untiring dissection soon proved Galen at error in many things. Vesalius completed his task at the early age of 28, and published his immortal work, the "Fabrica" in 1543.

How was he received? His book raised a perfect storm. Nearly everyone was against him for daring to question the authority of Galen. His own teacher, Sylvius, published a scathing attack. He continued his work, but things became so unpleasant for him that in a fit of discouragement he burned his manuscripts. Even later, in his position of private physician to Charles V, his critics persecuted him. Finally on the ridiculous pretext that the heart of a man on whom he was doing a post-mortem was seen to flutter, his enemies brought him before the inquisition, and he only escaped being put to death by the intervention of the king, and by promising to make a pilgrimage to the Holy Land. On his return he was shipwrecked and died. It is said he was in such penury that his remains would have been devoured by wild beasts had not a kind goldsmith paid his funeral charges.

Quite different was the treatment a few years later of Ambroise Paré whom we know now as one of the greatest surgeons of all time and a peer of Hunter and Lister Paré was the only Protestant to be spared in the massacre of St Bartholomew. Charles IX, "While crying kill, kill, wished to save no one except Master Ambroise Paré his first surgeon On the eve of the massacre he sent to seek him and for him to come to the royal chamber, commanding him not to budge from it, and said that it was not right that one who could save so many poor people should be thus massacred, and that he would not press him to change his religion any more than he would his nurse"

Paré, who was in a way as great an iconoclast as Vesalius, may be said to have met with more favourable contemporary criticism for two reasons, first because of his extraordinary personal magnetism and popularity, secondly because he was of immediate practical benefit to people

In the beginning of the 17th century came Harvey, as Welch remarks "bringing to light in the demonstration of the circulation of the blood the central fact of physiology" Although Galen had lost his anatomical throne to Vesalius he still ruled absolutely in all conceptions of the functions of the body It goes without saying that his discovery came out of the freedom of his mind, in keeping with the general liberation of intellect through the renaissance, his diligence in experimentation and observation, and finally it was made possible through that rare quality of mind we know as genius

Omitting any reference to his education, life and character, we pause and try to picture to ourselves the situation on that great day, April 17th, 1616, a week before Shakespeare's death, when William Harvey announced his discovery Osler paints for us very vividly the scene as Harvey stood before a small gathering and expounded his views before his fellows in the Royal College of Physicians Rumor had spread abroad about strange things to be expressed by the lecturer What were these men to think of young Harvey's ideas when they had been taught Galen's teaching, which said that the heart is a lamp, which is furnished with oil by the blood and air from the lungs, and that the liver was the source of the blood? Yet how were they to deny the truth of Harvey's experiment before their eyes? "Probably few in the lecture room" says Osler, "appreciated the full meaning of Harvey's words" It is unfortunate that we have no contemporary account of the impression made on some of the greater men present on that day Here we find an example of the natural inertia of men's minds It was too much for them Probably they loudly applauded his address but the true import of his words fell on barren ground Osler said that as far as he knew there was no reference to show that the lectures had any immediate influence on the profession, or that anybody outside of the few hearers ever heard about the matter at all But Harvey himself says "these views as usual pleased some, others less, some chid me and calumniated me and laid it to me as a crime that I had dared to depart from the precepts and

opinions of all anatomists " Their mental state we can only understand by a careful examination of the history and general thought at Harvey's time Such a heresy as a general circulation was too much for them

Although Harvey continued to experiment and expound his views without effect, he delayed twelve years any publication Osler says, "he seems to have belonged to that interesting type of men who know too much to write" That may be so, but after reading Harvey's introduction to his work which finally appeared, it strikes me that he really dreaded the inevitable prejudices and attacks of his contemporaries He must have had the persecution of Vesalius as a vivid example He was too great a genius

Sir Humphry Rolleston, in a recent essay, has brought to light the writings of two contemporaries of Harvey, viz, Thomas Winston and Henry Power In the case of the first man, a professor of anatomy at the College, it was shown that Harvey's doctrine was regarded as a fantastic idea, unworthy of serious attention and on the face of it absurd But Power's attitude was that of a faithful disciple of Harvey This contemporary however, was much younger than the first Just here it might be pointed out that it is usually the younger men who accept new ideas with the greatest favour, just as in young countries where the civilization is recent, *e g*, Russia, innovations are more readily acclaimed Although William Harvey saw the new doctrine established in England during his life-time, it continued to be bitterly opposed in France for nearly half a century

An important explanation of the poor acceptance of the discovery of the circulation is that there was nothing in it which was connected immediately into any practical value to people Men may sometimes embrace a discovery no matter how upsetting it is if they can see a distinct advantage or profit to come of it But the true merit of Harvey's work was not so much his demonstration of the circulation of the blood but his method, for with this start physiology became dynamic science "I am of the opinion" said Harvey, "that our first duty is to enquire whether a thing be or not before asking wherefore it is" Osler says, "It is pleasant to notice that our old friend Sir Thomas Browne, with his love of paradox declared that he preferred the circulation of the blood to the discovery of America"

That envy and jealousy have often played a part in criticism has been mentioned It was particularly so, it seems, in the lives of some of the men we are going to touch upon now In this connection perhaps it would not seem too much of a hyperbole to glance back into the realms of mythology, where we read how Aesculapius, the mythical father of the healing art, was treated by his contemporaries Even he was not exempt from jealousy, for we are told that when he became so proficient in his art that he was able even to raise Hippolytus from the dead, Jupiter, alarmed at this usurping of a gift of the Gods alone, slew him with a thunder-bolt

It has already been observed how discoveries of purely scientific interest were likely to be poorly received



It is to be noted too that the work of a genius who was obscure socially or professionally was more apt to escape notice or recognition. How then shall we account for the cold reception and the fifty years' neglect of an epoch-making discovery by a man who was a leading physician and an intimate friend of an emperor? Leopold Auenbrugger invented the art of percussion of the chest in 1753, practised it for seven years and then wrote a book about it. A small book it was, of ninety-five pages, but it will remain for ever as a medical classic.

Auenbrugger belonged to the Vienna School, but the Vienna School rejected him. We shall see that he was not the only genius they let slip by unrecognized. The men among whom he lived and worked never took up the discovery in spite of the fact that Auenbrugger practised it with great success and tried in his modest way to make the new method known. He remained entirely unappreciated until Corvisart in France, rediscovered Auenbrugger's art and translated his book. This was forty-seven years after its publication.

It was as a young man in his early thirties that Auenbrugger began to use percussion in his diagnostic work as physician in the finest hospital in Vienna at that time. It was not stumbled upon by chance, but was quite evidently a carefully worked-out clinical method, backed by an abundance of the keenest observations. To be convinced that it was the work of a genius one has only to read his little book, terse, to the point, a masterful recital of facts and deductions.

There is a good deal of sadness sur-

rounding these stories of medical discovery. Auenbrugger foresaw what his fate would be before he published his work. I shall quote the preface to his little book. It shows well his modesty as well as his foresight. "I here present the reader with a new sign which I have discovered for detecting diseases of the chest. This consists in the percussion of the human thorax, whereby, according to the character of the particular sounds thence elicited, an opinion is formed of the internal state of that cavity. In making public my discoveries respecting this matter I have been actuated neither by an itch for writing, nor a fondness for speculation, but by the desire of submitting to my brethren the fruits of seven years observations and reflection. In doing so I have not been unconscious of the dangers I must encounter, since it has always been the fate of those who have illustrated or improved the arts and sciences by their discoveries to be beset by envy, malice, hatred, detraction and calumny. This, the common lot I have chosen to undergo, but with the determination of refusing to everyone who is actuated by such motives as these all explanations of my doctrines." But then at the end he adds, "In submitting this to the public I doubt not that I shall be considered by all those who can justly appreciate medical science, as having thereby rendered a grateful service to our art, inasmuch as it must be allowed to throw no small degree of light upon the obscurer diseases of the chest, of which a more perfect knowledge has hitherto been much wanted."

Auenbrugger died in 1809 without ever seeing his work receive proper

recognition It is somewhat difficult to understand why such a valuable discovery was not accepted sooner We may state some factors however "Nearly every one of the great physicians of the time," says Garrison, "stood on a pedestal all his own, and many of these let it be known that they were in possession of private or secret remedies which were superior to all others" It was an age of system-makers and theorists Such individualism naturally did not favour the general reception of a seeming simple novelty as that of percussion It accounts too for the tendency to jealousy, that Auenbrugger mentions, which probably would have been less evident in any other age As factors in his criticism and neglect, then, we have on the one side the natural inherent inertia of men's minds toward anything new, coupled often with envy, and on the part of Auenbrugger an innate modesty and want of assertiveness, a certain serenity of nature, loving science for its own sake

So Auenbrugger was one of those unfortunate geniuses who discover a truth prematurely but are not gifted by nature with the ability to proclaim it convincingly to the world We shall consider presently another example of this in Semmelweis But after all, these men are compensated in a way. For surely the very consciousness of duty done must have sustained them I think it is safe to say that all really great discoveries were the outcome of pure scientific interest alone and did not come from trying for a practical result and material recompense Scientists, and physicians particularly, tend to become philosophical by the

steadying influences of everyday work The ubiquitous law of compensation so well extolled by Emerson must surely hold true here as elsewhere "So", says Weir Mitchell, "not even Marcus Aurelius himself could have been more content than Auenbrugger"

In all the history of medicine I doubt if there is a more extraordinary example of blind repudiation of a great discovery than is shown in the story of Ignaz Philipp Semmelweis At least twenty years before the work of Pasteur and Lister, Semmelweis broke through the shackles of tradition and current teaching and tried to show the world the cause and prevention of puerperal fever Childbed fever! It had been for centuries the stigma on the name of physicians and hospital practice "There are but two discoveries in medical history", says Sir William J Sinclair, "which were of the highest importance in producing *direct* and immediate blessings to the human race, by the saving of life and the prevention of suffering These were the discoveries of Edward Jenner in vaccination, and Semmelweis in puerperal fever." Of Jenner we have all heard much. Who then was this other genius? His story is so dramatic that it might not be amiss to dwell on it a little.

Briefly then, Semmelweis was born in Hungary in 1818 His school education was deficient, and this lack of mental discipline was a hindrance to him in the controversies of his later life He had an innate aversion to writing, we are told But he retained a natural eye with which to look into Nature, undimmed by the teaching of pedants In 1844 he graduated in med-

icine, and two years later assumed the duties of assistant at the First Obstetrical Clinic in the Vienna General Hospital

In order to make the work of Semmelweis quite clear it will be necessary to say a word about the hospital and the prevailing systems at the time. The Vienna Clinic was a great institution even at that time, the obstetrical division handling nearly 8000 cases a year. Fifty years before Semmelweis the English methods of midwifery were introduced, in which there was a minimum amount of handling of the women. But in 1822 a new professor began the teaching of obstetrics on the cadaver instead of the manikin. The students and doctors often proceeded straight from the post-mortem room to wards where they examined the patients without, of course, any antiseptic precautions. This practice continued, and when Semmelweis entered the hospital the mortality was appalling. In January 1844, two hundred and forty-two healthy women entered the No. I Obstetrical Clinic. Seventy-one died in spite of the best hospital treatment known then. About one in three died as the direct result of the introduction of virulent organisms into their bodies from the dirty and contaminated hands of the doctors.

Because of the warmth of his human sympathy the heart of Semmelweis was wrung by witnessing around him the suffering and death of thousands of the victims of some baleful agent which had eluded the efforts of generations of investigators to comprehend it. "Consider," says Carlyle, "how the beginning of all Thought worth the name is Love, and the wise

head never yet was without first the generous heart." It is not my purpose to give an account of the methods and work which led to the establishment of the etiology of puerperal fever. But let me assure you that the story might well be described as thrilling, and as Sinclair says, "It might remain of perennial value as an example of the application of logical method in working from the known to the unknown in medicine."

Consider the orthodox theories that Semmelweis had been taught regarding puerperal fever which he had to unlearn. It was maintained that it was a disease "*sui generis*", independent as an entity. Some thought it a milk fever, a milk peritonitis. Others thought it due to a contagion but that this thing assumed the form of a mysterious halo or areola which clung to the unfortunate practitioner who came under its malign influence, never guessing the real cause, filth and contamination from the post-mortem room. Everything from changes in the blood to changes in the weather were given as factors.

An important fact which continually presented a great problem to Semmelweis was as follows. The hospital was divided into two divisions, one for the students and one for the midwives. The midwives of course had little recourse to the post-mortem rooms, otherwise the conditions were about the same in both divisions. *But* the mortality of the first division was always at least three times that of the second. Why was this? With a never-ceasing zeal, Semmelweis attempted to find the answer. "Everywhere questions arose", he says, "everything re-

mained without explanation All was doubt and difficulty Only the great number of dead was an undoubted and terrible reality "

Next year, in 1847, a friend, Professor Kolletschka, while doing a post-mortem examination accidentally received a punctured wound in his finger What followed I recount in the words of Semmelweis himself "The professor thereupon became affected with lymphangitis, phlebitis in the upper extremity and he died from pleurisy, pericarditis, peritonitis and meningitis; and a few days before his death metastases occurred in one of the eyes In the excited condition in which I then was it rushed into my mind with irresistible clearness that the disease from which he had died was identical with that from which I had seen so many hundreds of lying-in women die The puerperal women also died from phlebitis, lymphangitis, peritonitis, pleuritis, meningitis, and in them also metastases sometimes occurred Day and night the vision of Kolletschka's malady haunted me and with ever increasing conviction I recognized the identity of the disease from which he died with the malady which I had observed to carry off so many women In his case the cause of the disease was the cadaveric material carried into the vascular system I must therefore put the question to myself did then the women I have seen die from an identical disease also have cadaveric matter carried into the vascular system? To this question I must answer yes "

Semmelweis did not wait He acted immediately He says, "In order to destroy the cadaveric material adher-

ing to the hands I began to employ a solution of chloride of lime, with which every doctor and student was required to wash his hands before making an examination The result was spectacular Within a few months the mortality of the first division fell below that of the second for the first time in the history of the hospital "

From then on his unceasing work led to more deductions, and he came nearer and nearer to the great discovery which Fate reserved for Lister How he found that puerperal fever was carried from an infected patient to others, how clinical events took their places in an orderly system in establishing the truth of his doctrine, these make an interesting story The explanation of why and how decomposed animal matter infects puerperae was to come with later developments of biological science, but the etiology, the cause, as discovered first by Semmelweis, stands today without essential modification as it was announced in 1847

Now for the reception Semmelweis had three influential friends, Hebra, Skoda and Rokitsansky who had followed his work and now championed his cause, giving him every encouragement to publish his results and doctrine Skoda, who was himself one of the greatest pioneers in auscultation and percussion had met with ill-usage by the Vienna School He became an object of derision, and all sorts of obstacles were placed in his way On the wretched pretext that Skoda hurt the patients and made them worse with his thumping and pressing on their chests he was transferred to the lunatic asylum to practice there Semmel-

weis showed the most lamentably poor judgment in the dissemination of his doctrine "He was in a sense his own worst enemy", says Sinclair. When he spoke he stirred up strife and controversies. For those great proud authorities of the day his doctrine was too simple. They refused to believe that the pathology of puerperal fever could be so easily explained. Imagine the control of the disease by simply washing the hands in chlorine water! Too firmly rooted in their minds was the old belief in mysterious, inexplicable, supernatural causes. Semmelweis was looked upon as a faddist. Then there was the inevitable jealousy, and the injury to the pride of men who thought themselves authorities, and who took the undiplomatic remarks of Semmelweis as personal affronts.

But with a chosen few, mostly younger men, the conception took root. Think how close Haller came to Lister's great discovery when in 1849, almost twenty years before the days of antiseptics he spoke of the immeasurable importance of the Semmelweis doctrine for surgery. This was probably the first time in the history of medicine that any suggestion was made regarding prophylaxis or antiseptics in surgery. Sinclair says, "The solemn, conventional professors smiled sarcastically at him. They looked upon Haller as a fantastic enthusiast, and treated his inspiration with contempt."

Semmelweis was completely misunderstood. He was ridiculed and persecuted. His mortification and indignation finally made him mentally unbalanced. He was practically driven from Vienna. Even Virchow sneered at him. The attacks of his enemies embittered

his existence and hurried him to the grave.

The extent to which small things and apparently unimportant circumstances have influenced the course of human events has been the subject of "wise saws and modern instances" of philosophers of all ages. In this case I think it is safe to say that if the counsels of Semmelweis had been followed, probably obstetrics instead of surgery would have initiated the greatest advance in medicine which has been made since the beginning of time. For the discoveries of bacteriology from Pasteur onwards, and the work of Lister, as Sinclair says, "only explained and confirmed." They were in no wise conflicting.

It seems to me that the reception of the Semmelweis doctrine must be explained under several headings. The first is personal partisan spirit. One cannot accuse the time and period of Semmelweis as being one of scientific stagnation, for there were great minds then. Nor yet was there blind adherence to tradition, for many old concepts were being overthrown. Nor did the doctrine conflict with religion or politics. But it was an age when a few great authorities were all-powerful. Their personal theories fought for acceptance. An upstart like Semmelweis with little professional or social position was bound to meet with enmity, when he attempted to overthrow all their elaborate theories. It was a personal affront. Yet it is astonishing that his proof of the saving of lives alone was not sufficiently compelling. Secondly the scientific thought of the day tended toward elaborate explanation. The doctrine of Semmelweis was

too simple for his great contemporaries. They must needs use long range glasses with which to look at nature, at the same time invoking the aid of mystical things to explain what they could not see between their ranges of vision. Lastly we should remember the personal deficiency of Semmelweis. He showed the poorest judgment in presenting his case. Had he had the personality of Lister or the literary ability of Oliver Wendell Holmes, his doctrine would probably have conquered Europe in a few months.

At this point let us review for a moment the story of an obscure monk who, seventy-five years ago made a hobby of growing peas in his cloister garden. He observed accurately what happened when different varieties were crossed, and then published his conclusions. These are as important to biology as atomic laws are to chemistry. The monk of course was Gregor Mendel and his discovery and conclusions are known as the Mendelian laws.

It is unnecessary to state here what Mendel's laws were, nor need their importance be stressed. I shall however, quote Professor Oertel who tells us that "quite apart from their great importance as regards heredity, they stand out as a cornerstone in biology because this monk first laid the foundations of experimental biology. The remarkable simplicity of his observations showed him as a true genius. He had neither laboratory nor preparatory education in the sciences. He had, being a priest, an excellent classical education and was a sharp thinker." Whether Professor Oertel believes he was a sharp thinker because of his

classical education is uncertain. It is a temptation to quote Hazlitt who says in his essay "On the Ignorance of the Learned", "anyone who has passed through the regular graduations of a classical education and is not made a fool by it may consider himself as having had a very narrow escape."

However what interests us here is the fact that not the slightest attention was paid to the great discovery, and so no use made of it for nearly fifty years, sixteen years after Mendel's death. Mendel fully realized the importance of his discovery for he published his work in an Austrian scientific journal in 1853. There it lay all during Darwin's time, when it could have been of so much value. Finally in 1900, de Vries rediscovered Mendel and confirmed his work. What more striking example could we have of genius unrecognized because the discoverer was by temperament not disposed to advertise or thrust his discovery upon a world which is too apt to be slow at accepting a new idea. It is true Mendel was somewhat isolated by reason of his social and even his geographical position. Nevertheless the outposts of the scientific world were asleep or blind. Even when his work at last came to light he was not immune from attacks, notably by Professor Weldon, who himself had done some work in this connection on the principles of heredity. That he tried to detract from Mendel's importance is putting it mildly. In commending Mendel he effectually "damned with faint praise"; so much so in fact that it led Professor Bateson to write a book, in defence of Mendel. That briefly, is the story of another great

mind "Voyaging through strange seas of thought alone"

Lord Lister What a name! Is it possible that a man whose work was so epoch-making could have met with anything but praise? What excuse could his critics find? Lister did not himself introduce any new radical theory The theory of antiseptis was known before his time History shows that great discoveries are rarely absolute novelties and that they have long existed as toys or curiosities We have seen how the work of Semmelweis twenty years before was really the same as that of Lister only more limited Semmelweis was a forerunner, but owing to his neglect was entirely unknown to Lister The germ theory in connection with disease, Pasteur introduced It was Lister who vitalized and dramatically proved the theory by demonstrating its practical value He simply introduced into surgery the principle of antiseptis It is said that before Lister 70% of all compound fractures and 50% of all major operations resulted in death As Professor Seelig remarks, "With one sweep this doleful picture was erased"

Lister's work then was of the greatest immediate practical value Yet in spite of this he met with a storm of bitter criticism A consideration of this could well be made the subject of a separate study I shall only mention a few points His critics might be put into two classes The first class includes men who stuck on certain non-essentials, as the early difficulties of operative technique, and who failed to grasp the great surgical principle It is astonishing that so great a man as Sir James Y Simpson who introduced

chloroform anesthesia in obstetrics should have been Lister's greatest opponent, even to the extent of envy and malice The other class of critics were those who were so utterly tied to old authority that they refused to believe either Pasteur's experiments or Lister's operative results, and considered any fundamental change in surgical practice as an insult to themselves, their practice, and the luminaries in whose train they followed We might recall many of the leaders of the age who took a decided stand against Lister For instance, even as late as 1869, the annual address in surgery to the British Medical Association given by Thomas Nunnely was devoted almost entirely to a denunciation of Lister It is reported at great length in the British Medical Journal for that year The main argument was that Lister had deserted the precepts of John Hunter "Lister's method", he says, "ignores those truths which formed the life-long labour of our great physiologist to establish" Nunnely absolutely opposed the germ theory, saying, "this speculation of organic germs is, I fear, far more than an innocent fallacy, its teaching will produce a positive injury" He ends by explaining suppuration of wounds as due to "vital conditions" and "those phases of unhealthy atmosphere or telluric influences" These were the words of one of England's greatest surgeons and a scientist only sixty years ago

It is interesting to note that these attacks were nearly always couched in the most flowery language which took the place of logical argument One is reminded of a couplet from Pope

"Words are like leaves, and where they most abound, much fruit of sense beneath is rarely found"

Pasteur's criticism would fill a book I shall only quote one example He had a long dispute with Pouchet about spontaneous generation Although eventually proved to be entirely wrong in his contention, Pouchet won his case at the time against Pasteur, was wildly acclaimed, and presented with a prize and membership in the Academy of Sciences

One more example shall we take Probably the most dramatic instance in the history of Science, of the degree to which authority and tradition influence contemporary opinion, is shown in the case of Charles Darwin In modern times surely no one man has produced such a revolution in scientific thought Whatever anticipation of the doctrines may be found in the writings of his predecessors "the broad facts remain", says Professor Seward, "that since the publication and by reason of the publication of 'Origin of the Species' in 1859, the fundamental conceptions and aims of the student of living nature have been completely changed"

It is undoubted that Darwin will always be considered a great genius, although not in the way that he was so much ahead of his time as some of the men we have considered I should say that if ever the world was ripe for a revolution in scientific thought it was when Charles Darwin touched the match to the fuse In proof of this there was the tremendous volume of scientific study and work along the Darwinian line which immediately followed The explosion which ensued

was by no means confined to biological thought. Psychology, ethics and cosmology were stirred to their foundations The upheaval that Darwinism caused in religious thought is notorious It is to the consideration of this latter that I shall confine most of my remarks here

To use a colloquial phrase Darwin "started something" in the religious world It is safe to say that this was farthest from his thought He was a scientist, pure and simple "I shall keep out of controversy", he said, "and just give my own facts." Only Truth was his star, and, to quote Hazlitt, "where the pursuit of truth has been the habitual study of any man's life, the love of truth will be his ruling passion" It is not the intention here to weary you with a review of the tremendous flood of religious criticism Two quotations taken at random will perhaps suffice to remind you of some of the controversies which raged The first was that of the greatest condemnation in viewing the scientific victory of Darwin "Never in the history of Man has so terrific a calamity befallen the race as that which all who look may behold, advancing as a deluge, black with destruction, resistless in might, uprooting our most cherished hopes, engulfing our most precious creed, and burying our highest life in mindless destruction." The second is a more favourable criticism "I submit that the more men know of actual Christian teaching, its fidelity to the past, and its sincerity in the face of discovery, the more certainly they will judge that the stimulus of doctrine of evolution has produced in the long run, vigour as well as flexi-



bility in the doctrine of the creation of man ”

A great new conception such as that of Darwinism, popularized as it soon became, was bound to influence the mass of people. Now religion, the adherence to faith, has been and is a fundamental part of people's minds. Carlyle says that a man's religion is the chief fact with regard to him. Anything which seemingly conflicts with this has in all ages caused a tremendous reaction. In earlier periods it has been at the bottom of the bitterest controversies and political strife, and indeed the bloodiest wars. But while it was inevitable that Darwinism should influence people's thought, religion, *as religion* should never have become mixed up in it. Nothing was surer than that the greatest misconceptions would arise. It became immediately a clash between *authorities*, the authority of religion and the authority of science. But — and here we come to the fundamental difference, and the eternal cause of strife — the authority of religion is Faith, and the authority of science is Fact and deduction in an objective way. Also in men's minds the reconciliation, if there is to be a reconciliation, must be brought about by their own intellectual methods.

In attempting to explain what I mean I shall quote from an essay of Hammerton's in which he discusses science and authority. He says, "Our men of science act, and the laws of scientific investigation compel them to act, as if it were not quite certain that the views of scientific subjects held by those early writers were so final as to render modern investigation superfluous. It is useless to disguise the

fact that there is real opposition of method between intellect and faith. All affirmations based upon authority must be treated as if they were doubtful. I mean that the man of science does not treat the affirmations of any priesthood with less respect than the affirmations of his own scientific brethren, he applies with perfect impartiality the same criticism to all affirmations from whatever source they emanate. The intellect does not recognize authority in anyone." I wish to emphasize here, and particularly in respect to Darwin, this factor of adherence to authority and tradition, because it is undoubtedly of the greatest importance in explaining criticism. Hammerton continues, "Whilst the scientist has no wish to offend those who believe in the infallibility of the author of Genesis, he is compelled to conduct his own investigations as if those infallibilities were matters of doubt and not of certainty." How Darwin was misunderstood! We have all heard how the laity accused him of attacking and attempting to overthrow biblical doctrines. Thus of course Darwin never did. He was a pure scientific investigator. Darwin was never dogmatic. If he challenged a certain rigidity of religious thought he did it all unconsciously. Hammerton concludes, "Although the intellectual (and scientific) methods are entirely independent of tradition, it may easily happen that the indirect results of our following those methods may be the overthrow of some dogma which has for generations been considered indispensable to man's spiritual welfare. With regard to this contingency it need only be observed that the intel-

lectual forces of humanity must act, like floods and winds, *according to their own laws*; and that if they cast down any edifice too weak to resist them, it must be because the original constructors had not built it substantially, or because those placed in charge of it had neglected to keep it in repair. This is their business, not ours. Our work is simply to ascertain truth by our own independent methods, alike without hostility to any persons claiming authority, and without deference to them."

That this was Darwin's method we cannot doubt. Nor can we doubt that it is the method of all geniuses of science. These forerunners of the truth were able to see clearly and to deduce correctly. Darwin tells us, "I have steadily endeavoured to keep my mind free so as to give up any hypothesis, however much beloved, as soon as facts are shown to be opposed to it." Again he says, "It is a golden rule, which I try to follow, to put every fact which is opposed to one's preconceived opinion in the strongest light. Absolute accuracy is the hardest merit to attain, and the highest merit. Any deviation is ruin."

This brings us practically to our own day. Times are changing. Probably the recognition and favourable reception of genius is much more likely to be immediate and sure now-a-days, than in the past. Osler illustrated this very nicely when he said, "It is interesting to compare the cordial welcome of the pallid spirochaete with the chilly reception of the tubercle bacillus." The reasons for this are many and would make an interesting study. We are better prepared to-day and dis-

coveries are immediately put to the test by experts. Possibly the danger of the present day is to be too credulous and to accept every wind of doctrine, mixing the dross with the gold. Bramwell of Edinburgh spoke of this not long ago in an address entitled "Progress of Medicine and the Retarding Influence of Credulity."

If it be true that human nature is essentially the same through the ages, then the geniuses of to-day and those yet unborn must face essentially the same forces of contemporary criticism. Great minds all too soon vanish into the grave. What a pity we cannot always recognize them while they are here. Science it is true builds forever, but the genius together with the charlatan and the fool is mortal and is soon lost to us.

This sketchy review far from attempts to cover the subject of "Medical Genius and Contemporary Criticism." It pretends to be only a faltering and, I fear, rambling introduction to a lengthy theme. It will have served its purpose however, if it has drawn our attention to an important aspect of the study of medical history. Really the best way to see a man is in the light of his time and generation. We are perhaps too apt to see the genius of history judged only by the standards of another time, the critics of another generation; to see back through the mists of time only the rugged peaks thrust above the fog, to escape the broad view of the barren plains and green foothills from which they rise. The man of genius, seen in his true perspective, appears indeed grander than ever.

## Editorials

### *THE FOURTEENTH ANNUAL MEETING*

The Fourteenth Annual Meeting has now become a matter of historical interest for the College, and very pleasant history at that, for it was a complete success in every way. With an attendance registering thirteen hundred it proved to be very little short of the Boston meeting, and this, considering the location and the season, speaks volumes for the intrinsic drawing value of these clinical sessions of the College. The program proved to be an unusually interesting one, quite the best one the College has ever had, and there were only one or two failures in attendance on the part of the speakers advertised. A large audience was present at all of the sessions, and listened with evident appreciation and interest. The first papers were somewhat marred by the inadequacy of the lantern service, which was promptly remedied, so that no further trouble was experienced to the end of the session. The voice-amplifiers worked unusually satisfactorily, indeed, and were about as perfect as such things can be, at this stage of their development. It must be said, however, that their use certainly makes of the speaker more or less an automatic machine, for the necessity of restricted movement in speaking directly into the microphone certainly cramps the individual style and spontaneity in address,

which, after all, constitute the things one wishes most to see in any public speaker. It becomes a question, whether the meetings that require the use of a large audience hall, with the necessity of using loud speakers, are not undesirable for this reason. Perhaps, as the College increases in size, the use of smaller lecture rooms with smaller sections, may offer the solution to this problem. Much praise was heard of the care with which the clinics had been prepared, and of the choice of material used in them. The exhibit was a great success, and its location in relation to the general meetings most advantageous, both for the exhibitor and the visitor. The Minneapolis men, and particularly Dr. Marx White, upon whom personally so much of the responsibility devolved, are to be sincerely congratulated for the great success of this meeting. Taken all in all, it led all of those that have preceded it, and establishes a new standard for those to follow.

### *THE APPARENT INCREASE IN THE INCIDENCE OF SYPHILITIC AORTITIS*

During the last several years there have appeared in the German literature various articles suggesting that under the modern arsenical treatment of syphilis there is actually taking place an *increasing* and *earlier incidence* of the so-called metaluetic

processes, such as leucoderma, aortitis, tabes and progressive paralysis, while on the other hand the tertiary skin lesions are less frequently encountered. The clinical face of syphilis seems to have essentially altered. Wilmans first called attention to the apparent increase in paresis and tabes; and although his conclusions have been confirmed by numerous syphilologists, they have been contradicted by nearly as many others. Langer<sup>\*</sup> has had an experience similar to that of Wilmans. While seeing many cases of primary syphilis, he has been struck by the fact that he has been seeing relatively few typical cases of secondary lues, which are being replaced by atypical, severe or malignant forms of syphilis. Leucoderma has become significantly more common, and even more marked has been the increase in cases of neurosyphilis, partly in the form of the so-called neurorecidive, partly as brain syphilis, paresis and tabes. On the other hand bone syphilis and gummatous organ-lues formerly so frequent have almost vanished out of the clinical picture. Further, there appears to be an increase in those cases resistant to therapy, according to reports by Jessner, Langer, Silberstein and others. It has become significant and of great practical value to check up these clinical impressions with the autopsy findings of the last decade in order to determine whether a pathologic-anatomic foundation exists for this apparent change in the clinical picture of syphilis. Langer analyzed the autopsy material at the Rudolf-

Virchow Krankenhaus, from the year 1905 to 1925, the number of autopsies occurring during this time being 23,015. Luetic stigmata were found in 1,268 of these, about 5.5 per cent. These stigmata were divided as to sex, 781 males and 487 females, 16 as many in the males as in the females. The highest incidence percentage of syphilitic stigmata occurred in 1919, when it rose to 9.07 per cent. The percentage relationship of aortitis to the total number of autopsies rose from 1.34 in 1906 to 3.69 per cent in 1925, but on the other hand the percentage relationship of aortitis to the syphilis-autopsies rose from 33.3 in 1906 to 83.87 in 1925, an increase of 2.5 fold, and of 2.7 fold for the total number of autopsies. Such an increase in the incidence of aortitis had been noted also by Jungmann and Hall. A separation of the two decades into 1906-1915 and 1916-1925 shows that the greater percentual increase of syphilis is in the second decade. Langer's table showing the ages of the patients showing syphilitic aortitis indicates that the life limit of the syphilitic has become shortened, confirming a previous observation by Melchior. The latter observer found in an observation of 358 cases of acquired syphilis a decrease of the life limit as compared to that of non-syphilitic cases. While among the syphilitics between the 30 and 60th years 65.4 per cent died, the percentage of deaths in the non-syphilitic cases for the same period was only 46 per cent. In Langer's material the peak of deaths in males, before and after 1915, was between 51-55 years; while in females before 1915 the peak was be-

<sup>\*</sup> LANGER, F. Münch. Med. Wochenschr., October, 1920, p. 1782.

tween 51-55 years, after 1915 it had sunk to 46-50 years. Langer further compares the incidence of aortitis with other luetic lesions of the liver, kidneys, respiratory organs, bones and genital organs. The organ most frequently affected, next to the aorta, was the liver. Before 1915 it was involved in 15.26 per cent of cases, after 1915 in only 8.46 per cent, a decline of 1.8 fold. Also the other organs showed after 1915 a drop in the incidence of luetic lesions. After 1915 the syphilitic lesions in other organs were associated usually with aortitis, before 1915 the great majority of such organ lesions occurred without aortitis. This confirms the observations made by Gurich to the effect that with the increase of aortitis, as well as of tabes and paresis, luetic disease of the other organs has sharply diminished in frequency of occurrence, and that the liver is most frequently involved next to the aorta, although in a much less percentage as compared to the aorta. Langer, therefore, argues with Gurich, Jungmann, Hall and other writers that in the course of the last two decades that aortic syphilis has greatly increased. With this view E. Fraenkel is in accord, and has advanced the question as to whether the increase in aortic syphilis may not be due to present day methods of therapy. On the other hand many clinical observers, Buschke, Finger, Fischer and others, on the ground of their experience with a large mass of clinical material have repeatedly advanced the view that the clinical picture of syphilis has undergone a great change, and that syphilis has wandered from the skin, and is now affecting the nerves and nervous

system. The comprehensive statistics founded upon a large material by Buschke and Schlarz confirm this view. We see fewer skin recidives than formerly, but so many more recidives in nervous and vascular systems. In this connection the findings of Heller in regard to aneurysms are interesting. In the years 1859-1870 there were 4.3 per cent aneurysms as against 19.2 per cent in the years 1910-1914, that is, the number of aneurysms increased in 1910-1914 more than four fold. From the psychiatric side the increase in the incidence of aneurysm has been confirmed. Coenen, Frisch and Loewenberg state that aortitis occurs in 39 per cent of cases of paresis and 33 per cent of cases of tabes. Copolla found involvement of the aorta in 86.93 per cent of cases of paralysis and tabes. Coenen made the observation that involvement of the aorta in tabes and paresis had risen from 2.2 per cent in the years 1908-1914 to 4.29 per cent in the years 1919-1925, almost a doubled incidence. On the other hand almost all clinicians have noted the decrease in tertiary skin lues. While the elder Glueck in the years 1898-1902 saw tertiary lues in 23 per cent of 15,064 syphilitics, the younger Glueck in the years 1913-1922 saw tertiary lues in only 2.1 per cent of 2,377 syphilitics. Formerly aortitis was very rare in Morocco, aortic aneurysm being unknown, but Durop and Salle have recently reported two cases of this condition there. Jungmann and Hall have attempted to show the relationship of the increase of aortitis to constitutional factors, and affirm that men of pyknic habitus

show aortic lues, as well as paresis, while the tabetics are asthenics in about 50 per cent of cases. While these observations are interesting they throw no light upon the increase of late syphilitic lesions in aorta and central nervous system. It will be well to bear in mind the warnings of Buschke made at the beginning of the salvarsan era of therapy; apparently many of them have been fulfilled. Not only have paralysis and tabes increased, according to Wilmans, but aortic syphilis has increased about three fold. Wilmans holds that the modern antisyphilitic treatment is indeed the cause of the change in the clinical picture of syphilis, in that it produces in the affected individual a shortening of the interval between the infection and the first clinical symptoms. Jungmann and Hall show in their Arbeit that in untreated cases an average of 23.4 years occurs before the advent of syphilitic organic disease; in insufficiently treated cases an average of 22.1 years, while in fully treated cases an average of 15.0 years occurs. The clinical observations of Jungmann and Hall appear to show

that the modern therapy of syphilis appears to shorten the interval between infection and the first appearance of aortic lues, as also of central nervous system lues. What the modern therapy of syphilis has accomplished would appear to be the prompt disappearance of the skin lesions, and the greater rarity of bone and gummatous organ-lesions. When we compare the importance of a gumma of the skin, bone or liver with the much more important syphilis of the aorta and central nervous system, the former is usually easily controlled by simple medication, but the patient with aortitis, paresis or tabes in spite of salvarsan therapy, in spite of malaria therapy, or other fever treatment, will still be with us as a spectre of the disease. Langer closes his paper with a plea for a more rational therapy of syphilis—not that which will be the most intensive spirochaeticidal agent, but that which will least disturb the immunity processes of the body. He believes in the mildest treatment possible, which will aid and support the body in its defensive processes.

## Abstracts

*The Effect of a Suprarenal Extract for Malignant Growth* By WALTER B COFFEY and JOHN D HUMBER (J A M A Feb 1, 1930, p 359)

In a report made to the San Francisco County Pathological Society, January 6, these authors pointed out that their experimental work with endocrine extracts began in 1925, in the attempt to find a vasodilator and a stabilizer of tissue growth. After many failures, an extract of suprarenal cortex from sheep was made which reduced blood pressure when injected subcutaneously. Further development of the work demonstrated that this extract was a stabilizer of growth. A few patients with high blood pressure together with a malignant condition had under treatment a lowering of blood pressure from 240 to 150, together with a sloughing of the malignant tissue and subsequent disappearance of the growth. Later, they injected the extract only in patients with inoperable malignant growth, in the possibility of obtaining autopsies. One patient who had an embryonal carcinoma of the testes which could not be completely removed, was given the first injection, August 22, 1927, and is now without any evidence of neoplasm. Another patient with inoperable carcinoma of the rectum and complete obstruction was referred for colostomy, and was given a first injection, Sept 1, 1929. At present this patient is without any evidence of tumor and so far has had no ill effects from the injections, and has apparently recovered. Within from 24-48 hours after the first dose, the tumor masses begin to soften, then liquefy, and within 10 days begin to slough. When the masses are favorably located, many have begun to slough within 48 hours. Although their series to date is small, they have had an opportunity to study the changes in the tissues of patients who died. The tissues are studied by Dr A M Moody. The essential

changes are necrosis of tumor cells which cannot at present be differentiated from that occurring naturally in malignant tumors. In one case of primary carcinoma of the kidney, with metastases in the lungs, about the necrotic secondary tumor nodules, there was marked vascularization. One patient who had received injections for two and a half months prior to death, and who died from renal insufficiency as the result of bilateral ureteral obstruction, had atrophic suprarenals, measuring only 3 mm in thickness. The patient had a primary carcinoma of the cervix, which during the course of the injections had sloughed away. No secondary growths beyond the uterus and bladder were present. The writers emphasize the fact that their work to date has been purely experimental. Softening with liquefaction has occurred in all tumors thus far studied. These tumors except one, were all carcinomas of varying types, the one exception was a spindle cell sarcoma. They wish to impress upon the medical profession the fact that the work to date, which they style "quite promising" is still in the experimental stage, and therefore decidedly inconclusive.

*An Interpretation of Malignant Growth Based on the Chemistry of Cell Division* By FREDERICK S HAMMETT (Arch of Pathol, October, 1929, p 575)

Proliferation of cells is the common defining characteristic of all malignant growth. It follows then that the problem of malignancy centers itself primarily on the processes of cell reproduction. The question of inciting agents is secondary, since all these produce but one biologic reaction, namely, cell proliferation. Once the chain of reactions leading to increase in cell number has been set off in a receptive field, further development depends on the intrinsic biologic characteristics of the tissue in which the growth is taking place, regardless of the

nature of the agent which upsets the previously existing equilibrium. It is clear that the most logical way to approach the problem is through a study of the chemical processes specified for growth by increase in cell number. The first step was a description of the experimental work leading to a demonstration that the sulphhydryl group is the essential stimulus to multiplication of cells in healthy material. Direct transference of this observation to tumor tissue is allowable on the basis of Baker's report that glutathione, a sulphhydryl-containing compound is stimulative of a proliferation of cells in tissue cultures of sarcomatous fibroblasts. The next step was an examination of the available reports with respect to sulphur metabolism in general and sulphhydryl in particular in tumor-bearing persons and tumor tissue. From this, it was seen that the correlative data consistently support the idea of an inter-relationship between sulphhydryl and malignancy. The third step was an examination of the etiologic concepts of malignancy for the purpose of seeing whether or not they could be lined up on a common basis. From the known facts the thesis was developed that malignancy, in general, is a product of a combination and constitutional and acquired factors. An analysis of these showed that their influence is interpretable in terms of sulphhydryl. The chief manifestations of malignancy were also tested against this concept and found to be sustaining thereof. From all this the generalization has developed that the potentiality for malignancy lies in the hereditary determination of lines of cells retaining the embryonic characteristics of a heightened sensitivity to the essential stimulus to cell-proliferation, sulphhydryl, and that the development of malignancy depends on the presentation to the potentially tumor-producing cells of an adequate concentration of this chemical group. The author is willing to admit that this interpretation is possibly not the last word in the apparently complex problem of malignant disease. On the other hand, it does suffice to bring some order out of a previously existing chaos. Its validity, however, rests on the soundness of the biological principles involved.

*The Significance of Balint's Phenomenon in Ulcer Patients* By S. A. WESTRA (Klin Wschnschr., Sept., 1929, p. 1808)

In 1926 and 1927 Balint published an article and monograph in which he advanced the view that patients with gastric and duodenal ulcers have a more marked acid reaction in their tissues than normal individuals. Since this view was widely received and became the basis for various methods of treatment, Westra considered it advisable to subject the data on which this hypothesis was based to further critical experimentation. Balint injected intravenously 20 ccm of an 8% sodium bicarbonate solution and estimated the pH and the titration-acidity in the urine for two hours preceding and two hours following the infusion, in fasting patients. It showed then that the urine became more alkaline, but that the difference in the ulcer-patients is much less than in the case of the control patients. Among the ulcer patients there were some in whom after the infusion of carbonate there was no increase of the urine alkalinity. This is the Balint phenomenon and Balint explained it as due to a bicarbonate retention on the part of the tissue, which would indicate an acid reaction in the tissue. On the grounds of his experimental work Westra concludes that the occurrence of Balint's phenomenon in individual ulcer cases is confirmed. It depends however upon changes of acidity in the urine and not upon a more rapid disappearance of the infused alkali from the blood. Bicarbonate infusions produce no alkalinity of the tissues, but through their influence on the autonomous nervous system produce a stimulation of the vagus. The Balint hypothesis of a tissue-acidity in ulcer patients is not confirmed. The Balint phenomenon finds a satisfactory explanation in the vagotonus of the ulcer patient, and there is no ground for the assumption of a theory of tissue acidosis in addition to the vagotonus theory of *ulcus ventriculi* and *duodeni*.

*The Kahn Precipitation Test in Infancy and in Early Childhood* By JOHN COFFEY and KATHERINE V. KREIDER, (Amer Jour of Dis of Child, December, 1929, p. 1206).

Comparisons of the standard Noguchi Wassermann modification with the standard



Kahn test were carried out on 1,185 infants and young children under investigation for syphilis, 43 patients under treatment for syphilis and 315 mothers of patients in the aforementioned groups. The results of this study showed that the Kahn test is a highly sensitive and highly specific serologic test in infancy and early childhood. The reaction closely parallels the Wassermann reaction, but is not identical with it. Positive Wassermann reactions are more easily reversed by antisyphilitic therapy than are positive Kahn reactions. The Kahn test is considerably more sensitive than the Wassermann test in mothers of syphilitic offspring. It is highly specific in mothers of non-syphilitic offspring and equals the Wassermann test in this regard. The Kahn test has decided advantages in simplicity as a laboratory procedure. The Kahn test performed alone would have given slightly more reliable information than the Wassermann test performed alone on this group of patients. The performance of both complement fixation and precipitation tests simultaneously on identical serums gives more information than either test alone and affords a dual control in serologic diagnosis, which seems desirable.

*The Importance of Indicanuria, Stool Fat and Schmidt Fermentation Test in the Practice of Pediatrics* By R. G. FREEMAN, E. G. MILLER, and R. G. FREEMAN, JR. (*Arch of Ped*, May, 1929, p. 269)

In cases of digestive disturbance in children it is desirable to obtain all possible information regarding the cause, and much knowledge regarding the sort and amount of food that an individual child can care for, can be obtained by examination of his urine and feces. For a number of years tests for indican in the urine, chemical analysis of stools for fat and a Schmidt fermentation test have been carried out as routine tests in practice, and it has been possible to make satisfactory adjustments of the diet of children with malnutrition and digestive symptoms on the basis of the findings of those tests. Obermayer's method is used for the test for indican in the urine. The fecal fat was determined by the method of Freeman and Miller. As a result of this study it was found that the tests used for

indican, fecal fat and fermentation are sufficiently accurate and simple to be used as office routine in all cases in which symptoms of digestive disturbance in children are evident. These tests also indicate the character of the food that is the source of trouble, and also serve as an excellent control of the results of treatment. This study indicates that normal children show infrequent indicanuria, fecal fat under 65 per cent, and fermentation tests producing less than 7 cc, while children with symptoms of abnormal alimentation practically always show either an indicanuria, an excess of stool fat, or fermentation by the Schmidt test, and in some cases all three of these. 80 per cent of the examinations in children with symptoms, in office practice, showed carbohydrate excess, 60 per cent protein excess, and 33 per cent fat excess. Dietary restriction of these cases, in accordance with our laboratory findings (if carried out conscientiously by the parents or others in charge of the children) usually result in improvement in the condition of the children, and in a reduction of the abnormalities in the urine and feces. The occurrence of indican in so-called normal children is considerably less than in those examined for symptoms of indigestion. Although there is no proof, the authors feel strongly that the incidence of the indican in the normal group was due to transient digestive upsets.

*Silicosis Among Rock Drillers, Blasters and Excavators in New York City* By ADELAIDE ROSS SMITH (*Jour of Indust Hygiene*, Feb., 1929)

As an occupational disease, silicosis has a long history, but it is only comparatively recently, that is to say, within the past twenty-five years, that it has received attention. In the United States the first studies of silicosis were made among the zinc miners of Missouri by Lanza and Childs, in 1917. The present study was made of 208 rock drillers, blasters and excavators in New York City for the purpose of determining the incidence of silicosis among them. Silicosis was found to be present in 118, or in 57 per cent of the men examined. Twenty-three per cent of the men examined showed radiographic evidence of antepimary sili-

cosis, 19 per cent of first stage silicosis, 7 per cent of second stage silicosis, and 8 per cent of third stage silicosis. Blasters, rock drillers and excavators were affected by the disease in frequency and in severity in the order named. Second and third stage silicosis occurred four times as frequently among those who had done under-ground work, as among those who had done only open excavating. The incidence of silicosis among men who had worked only in New York City was slightly higher than among those who had worked elsewhere as well. Ante-primary silicosis was found to be present in conspicuous proportions after five years' exposure to rock dust, first stage silicosis after ten years' exposure, and second and third stage silicosis after twenty years' exposure. Second and third stage silicosis was associated to a noticeable degree

with a past history of pleurisy and pneumonia. Dyspnea and expectoration were the only symptoms found to be significantly associated with the disease in this study. Lung signs were in general inclusive, although râles and diminished resonance and breath sounds were found most frequently among those showing silicosis in the second and third stages. Tuberculous lesions revealed by roentgen examination, including both those considered active, and those believed to be probably healed, occurred in nineteen cases, or 9 per cent of the total number. The incidence of all tuberculous lesions was approximately three times as high in the group of cases showing second and third stage silicosis as in any of the other groups. The author concludes that silicosis constitutes a serious health hazard to rock drillers, blasters, and excavators in New York City.

## Reviews

*Grenz Ray Therapy* By GUSTAV BUCKY, M.D., New York, with contributions by DR OTTO GLASSER, Cleveland, and DR OLGA BECKER-MANHEIMER, Hamburg. Translated by WALTER JAMES HIGHMAN, M.D., New York. 170 pages, 40 illustrations in the text. The McMillan Company, New York, 1929. Price in cloth, \$3.50.

Grenz rays are soft Roentgen rays having wave lengths of from 1-3 Angstrom units and are produced in lithium glass x-ray tubes with voltages from 4-10 kilovolts. They are called Grenz or border-line rays to express the fact that they border on the utilizable Roentgen wave length. This book discusses the exact position of the Grenz ray spectrum in the general spectrum of radiation, and describes the high tension apparatus, and tubes for their production. Grenz rays are so soft that they are absorbed in air to considerable degree. Therefore, only direct determinations of the radiation quality and quantity at the site of application are found to be satisfactory. The absorption of Grenz rays in aluminum foil of 0.0125 mm thickness has been determined for different conditions of radiation and the half-value layers of this radiations are found to be between 0.007 and 0.04 mm of aluminum. The effective wave lengths are found to lie between 1 and 3 Angstrom units. Data for translating half-value layers of aluminum into half-value layers of air, water, muscle, cutis vera, epidermis and subcutaneous tissue are given. The method of standardizing the intensity of Grenz rays in R units per minute is described. A description is given of a small, 1 cc, ionization chamber of goldbeater's skin which is practical for dosage measurements in Grenz rays and which can be connected to any ionization Roentgen dosimeter, and shows no appreciable absorption and can be used to measure the radiation intensity of Grenz

rays independent of the wave length down to rays produced at 5 kilovolts. The threshold erythema dose for Grenz rays seems to be in the neighborhood of 300 R units. A chapter is given to anatomic and biologic considerations of the effects of Grenz rays. No arbitrary conclusions as to biological differences between the effect of Grenz and Roentgen rays are yet warranted. The technique of Grenz rays therapy is described, and a chapter is given on the clinical symptoms in Grenz ray therapy. The clinical effects on the skin after exposure to Grenz rays are characteristic and differ materially from those encountered after the Roentgen ray, some resemble more those produced by Roentgen rays, while others resemble those seen after exposure to ultraviolet rays. The author considers the most important effects of Grenz rays to be their influence on endocrine secretion, their antispastic and stimulating effects. Grenz ray treatment of skin and internal conditions never produces by-effects as Roentgen rays do. He further claims that expert application of Grenz rays has not hitherto produced sequelae in a single instance, and that the danger coefficient of Grenz rays is not to be compared with that of the Roentgen ray. If future experimental work should confirm this, it is possible that the Grenz ray may come to replace the Roentgen ray in a large proportion of cases. The whole matter, however, is still in an early experimental stage, and no positive conclusions are as yet warranted.

*Practical Massage and Corrective Exercises With Applied Anatomy* By HARTVIG NISSEN, Late President of Posse Normal School of Gymnastics, For Twenty-four Years Lecturer and Instructor of Massage and Swedish Gymnastics at Harvard University Summer School, etc. Fifth Edition, Revised and Enlarged by HARRY NISSEN, President, Posse-Nissen School

of Physical Education, Boston, Mass 271 pages, 72 original half-tone and line engravings F A Davis Company, Philadelphia, 1929 Price in cloth, \$2.50

This little book has been used as a textbook at the Posse-Nissen School of Physical Education for the past twelve years It has now been carefully revised in order that certain parts may be made clearer and more helpful through the addition of new material, new illustrations and lists of exercises It is divided into three parts for ease of study—First, the different manipulations and their effects, Second, applied anatomy and corrective exercises with various lists of exercises, Third, treatment of various diseases and injuries, including a discussion on flat foot The theory and art of massage and corrective exercises are concisely and clearly described and explained, and illustrated by numerous well-chosen illustrations It contains very useful knowledge for the practitioner, who can utilize in his daily practice the methods herein described with great practical value to his patients, as, for example, in the indicated treatment for lumbago, a condition which every physician is frequently called upon to treat

*Materia Medica and Therapeutics Including Pharmacy and Pharmacology* By REYNOLD WEBB WILSON, M.A., M.D., LL.D., D.C.L. Twelfth Edition, Revised in accordance with the United States Pharmacopoeia X and the National Formulary V With an Index of Symptoms and Diseases 600 pages P Blakiston's Son and Company, Inc., Philadelphia, 1929 Price in cloth, \$5.00 net

The appearance of the United States Pharmacopoeia X has necessitated a rewriting of the section devoted to Pharmacy and Materia Medica and a thorough revision of this volume, which treats of the official drugs and preparations only, with such incidental reference to non-official as their usage warrants Every effort has been made toward condensation, as far as compatible with clearness In order that the subjects might be presented in one volume and all repetitions avoided, cross references have been inserted, and an exhaustive index added for the convenience of physicians who use

this book as a reference The many advances have necessitated the division of the work into two parts, the first being devoted to Materia Medica and Pharmacy, in which full attention is given to pharmaceutical processes, to the various kinds of preparations, with their dosage and to the art of prescribing, after which the description of remedies is taken up in detail These are divided into two sections the Inorganic and the Organic Materia Medica The general classification adopted is one based on the grouping of the articles according to the chemical or physiological divisions to which each belongs The course of instruction in Materia Medica should include the performance of the simpler pharmaceutical operations, demonstration of the drugs and their preparations, and practice in prescription writing It is believed that it is best to learn first the nature of the substance, and then its action and uses in medicine In the second part which deals with Pharmacology and Therapeutics, the classification employed is based on the particular physiological system upon which the various agents principally act There is a complete presentation of the official remedies and very elaborate descriptions of their pharmacological action and therapeutic uses In these descriptions the effort has been made to present the latest views of the highest authorities in these departments, and to render the book as practically useful as possible by full details regarding treatment which have been found to be valuable in actual practice In the National Formulary are contained many preparations which have the sanction of general use These have been freely commented upon because they are efficient and agreeable for prescribing, and through their use the resources of the practitioner will be greatly enlarged It is believed that this volume offers to the medical student and to the practitioner, a very complete presentation of the resources of Materia Medica, of their Pharmacology and their application in Therapeutics A critical survey of the contents confirms the author's aims and belief, and the volume may be recommended as a well-organized and condensed work, covering the ground sufficiently thoroughly, for the purposes indicated

*Hypertension and Nephritis* By ARTHUR M FISHBERG, M D, Adjunct Attending Physician to Mount Sinai and Montefiore Hospitals, New York City 566 pages, 33 engravings and 1 colored plate Lea and Febiger, Philadelphia, 1930 Price, \$6 50 net

The purpose of this work is to depict our present knowledge of the heterogeneous group of diseases traditionally included in the concept of Bright's disease. It is written primarily from the point of view of the actual practice of medicine, and aims to summarize for the practitioner the information that practice, clinic and laboratory have yielded regarding the hypertensive and renal diseases. In the century that has elapsed since the classical memoir of Bright, hypertension and nephritis have occupied focal points of medical interest, and in recent years they have been more than ever in the foreground. The introduction of the sphygmomanometer into general practice has revealed the great frequency of essential hypertension, and these is good reason to believe that its incidence is increasing. Recent development of various chemical and physico-chemical methods of investigation renders feasible the fruitful study of many fundamental problems presented by the renal and hypertension diseases which were previously not open to attack. Understanding of the hypertensive and renal diseases has been greatly advanced by the correlation of laboratory investigations with bedside and post-mortem studies. Progress has not been solely along theoretical lines, but the actual practice of diagnosis, prognosis and treatment has been notably furthered. This work is written primarily for the general practitioner whose laboratory facilities are usually limited. Therefore, diagnosis by clinical methods has been stressed. Particular attention has been given to symptomatology, and understanding of which is essential to accurate diagnosis. Relatively simple dietetic measures are recommended in the section on treatment, dietaries which can be supplied in the home of the patient under the direction of the family physician. Throughout the book the author has kept the general practitioner in mind, recommending such tests and other procedures as can be easily

carried out by him. For example, the simple specific gravity test is, in the author's opinion, the best method at present available for studying the functional capacity of the kidneys, and a simple technique is given for this test which is well adapted to general practice. It is emphasized that study of the blood chemistry is necessary in only a minority of patients with high blood pressure, and that when it is desirable as much information concerning the excretory capacity of the kidneys is furnished by the determination of either the urea or the non-protein nitrogen content of the blood as by more detailed and involved studies. The table of contents shows a thorough grasp of the subject and the comprehensive nature of the ground covered in this book. The material is clearly presented, and the illustrations are very fair. Altogether the work forms a very satisfactory presentation of the subjects of hypertension, nephrosis and nephritis.

*The Blood Picture and Its Clinical Significance (Including Tropical Diseases)* A Guidebook on the Microscopy of Blood By PROFESSOR DR VICTOR SCHILLING, Physician-in-Chief, The First Medical University Clinic, Charité, Berlin. Translated and Edited by R B H GRADVOHL, M D, Director of the Pasteur Institute of St Louis and the Gradwohl School of Laboratory Technique, St Louis, Mo. Seventh and Eighth Revised Editions. 408 pages, 44 illustrations and 4 color plates. The C V Mosby Company, St Louis, 1929. Price in cloth, \$10 00.

This book is based upon the author's own practical experience. In its first edition, in 1912, it appealed primarily to physicians practicing in the tropics. In later editions it was enlarged and supplemented by numerous practical examples from the whole field of medicine. An understanding of the blood picture should no longer be a rare art, but rather a routine procedure, familiar to all physicians. It is not intended to replace the well-known manuals of hematology, but rather to supplement them, by simplifying existing methods, to the exclusion of all superfluous material, and to assist in our understanding of the morphology of the

blood picture In this work the blood picture is purposely put in the foreground, so that its symptomatic, prognostic or diagnostic value for known and unknown diseases may be tested In the author's opinion, the importance of the blood picture has materially advanced, sufficiently to take rank with the fundamental bedside methods of examination, with pulse records, fever curves, urine examination, auscultation and percussion It has become a necessary part of a medical examination in all doubtful or difficult cases In this edition there have been added to the sections on blood typing, the "Guttadiaphot method," a discussion of Arneith's new book on "Qualitative Blood Theory," and the Bartonella group and erythrocytes have also been added The paragraphs on the sedimentation reaction have been enlarged Changes in the protoplasm of leucocytes has also been rewritten Liver therapy in pernicious anemia, and a few rare blood pictures, such as malignant neutropenia, aleukia, etc, have also been added Otherwise the fundamental features of the book remain practically the same as in the first edition It is a work of value for the laboratory worker in internal medicine when used in connection with other manuals of hematology

*Old Age, The Major Involution The Physiology and Pathology of the Aging Process*  
By ALDRICH SCOTT WARTHIN, Ph D, M D, LL D, Professor of Pathology and Director of the Pathological Laboratories in the University of Michigan, Ann Arbor  
With 199 pages and 29 illustrations Paul B Hoeber, Inc, New York, 1929 Price in cloth, \$3.00 Special limited edition, \$12.50

"I have read the book from cover to cover I have not only been interested I have profited You definitely establish your thesis I do not see how any one with a knowledge of science, and especially with a knowledge of the human body can deny your major statements You speak with such evident first hand knowledge, with so much reserve, yet with such positiveness, you marshal your proof in such an orderly way, as to be convincing Moreover, you do this with such clarity, with such excellent choice and arrangement of words that your writing has

a grace and charm—a style men call it—that it enables one to read with pleasure I congratulate you on the book I only wish I had the knowledge, ability, time and urge to write something as good I have not been depressed by your dwelling upon the inevitableness of old age Perhaps this is because I have long viewed age in that light I have not been depressed even when I read your catalogue of the features of fully developed senility You must know how heartily I endorse your praise of gardening as an avocation Practiced in an amateurish and somewhat irregular way, it has been of inestimable help in keeping me physically fit and in preserving—so it seems to me—an optimistic view of life Though I don't understand the philosophy and full meaning of life, I have learned many things concerning it by communion with plants and the soil May I venture to give two quotations that I enjoy repeating to myself The first is from Kipling —

"The cure for this ill is not to sit still  
And frowst with a book by the fire,  
But to take a large hoe, and a shovel also,  
And dig till you gently perspire"

The other is the last sentence of Voltaire's *Candide* —

"All that is very well," answered Candide, "but let us cultivate our garden"

There is comfort in having scientific assurance that the aging process in the brain, as shown by mental and spiritual functions, is not always as advanced as that in some other organs of the body I am hoping that when I am older in years and perhaps badly shattered in body, as I sit comfortably slippered in a warm corner of the fireside with a good book, and a few tried friends who endure a not too personally reminiscent garrulousness because it is mixed with serenity and a grain of wisdom that has come from experience and a sane view of life, I am hoping that then it may be said to me as the Italian proverb has it—"Vale più un vecchio in un canto che un giovane in un campo"—An old man in a corner is worth more than a young man in the field And my dear Warthin, may I wish the same serene old age for you!"

James B Herrick  
(Happy, indeed, is he who receives such a letter—A S W)

## College News Notes

At the General Business Meeting of the American College of Physicians held at Minneapolis, February 13, in connection with the Fourteenth Annual Clinical Session, the following Officers, Regents and Governors were elected

### OFFICERS

President	Sydney R Miller, Baltimore Md
President-Elect	S Marx White Minneapolis, Minn
First Vice President	Aldred Scott Warthin, Ann Arbor, Mich
Second Vice President	F M Pottenger, Monrovia, Calif

### REGENTS

James B Herrick	TERM EXPIRING 1931	Chicago, Ill
Logan Clendenning	TERM EXPIRING 1932	Kansas City, Mo
James R Arneill	TERM EXPIRING 1933	Denver, Colo
Walter L Bierring		Des Moines Iowa
George E Brown		Rochester, Minn
John H Musser		New Orleans, La
O H Perry Pepper		Philadelphia, Pa

### BOARD OF GOVERNORS

Wm H Deaderick	TERM EXPIRING 1933	Hot Springs, Ark
Hans Lisser		San Francisco, Calif (Northern)
Tom Bentley Throckmorton		Des Moines Iowa
Randolph Lyons		New Orleans, La
Charles G Jennings		Detroit, Mich
Edward L Tuohy		Duluth, Minn
A Comingo Griffith		Kansas City, Mo
Edward O Otis		Exeter, N H
W Blair Stewart		Atlantic City, N J
Charles H Cocke		Asheville, N C
Julius O Arnson		Bismarck, N D
Fred J Farnell		Providence, R I
Robert Wilson, Jr		Charleston, S C
Clarence H Beecher		Burlington, Vt
J M Hutcheson		Richmond, Va
Frederick Epplen		Seattle, Wash
John N Simpson		Morgantown, W Va
D Slater Lewis		Montreal, Que

At the organization of the new Board of Governors on February 14, Dr Charles G Jennings, of Detroit, Mich, retired as Chairman of the Board Dr W Blair Stewart, Atlantic City, N J, was elected successor to Dr Jennings, and thereby becomes a member ex officio of the Board of Regents

At the meeting of the new Board of Regents on February 14, the following were elected members of the Executive Committee for 1930-31

Sydney R Miller	Baltimore, Md
Clement R Jones	Pittsburgh, Pa
Jonathan C Meakins	Montreal, Que
James H Means	Boston, Mass
James Alex Miller	New York, N Y
George Morris Piersol	Philadelphia, Pa
Maurice C Pincoffs	Baltimore, Md
Aldred Scott Warthin	Ann Arbor, Mich
S Marx White	Minneapolis, Minn

The Board of Regents, in accordance with the provisions of the By-Laws, appointed Dr George Morris Piersol, Philadelphia, Pa, Secretary-General, and Dr Clement R Jones, Pittsburgh, Pa, Treasurer for the year 1930-31

At the 1930 Annual Convocation of the College at Minneapolis on February 12, the following physicians were regularly inducted to Fellowship During the processional, the Officers, Regents and elected candidates marched to their places in the Auditorium The candidates were presented by Dr George Morris Piersol, Secretary-General of the College, after the administration of the Fellowship Pledge by Dr F M Pottenger, Fellowships were conferred by Dr John H Musser, retiring President The annual address of the President which will be printed later in this journal, was delivered by President Musser Following adjournment, the newly inducted Fellows signed the official Roster and received their Certificates of membership The entire Convocation Program was dignified and impressive

F Dennette Adams	Boston, Mass
Winthrop Adams	Washington, D C
Thomas Addis	San Francisco, Calif
Frank Nathaniel Allan	Rochester, Minn
Olin Sudler Allen	Wilmington, Del
Harry L Arnold	Honolulu, Hawaii
J Richards Aurchus	St Paul, Minn
Samuel Ayres, Jr	Los Angeles, Calif
Henry T Ballantine	Muskogee, Okla
Gabel Marion Balph	Philadelphia, Pa
Archie Ray Barnes	Rochester, Minn
Frederick Rigby Barnes	Fall River, Mass
Harold Ludlow Barnes	Brooklyn, N Y
Oscar B Biern	Huntington, W Va
Arthur I Bloominfeld	San Francisco, Calif
Andrew Bondhus	Pasadena, Calif
Walter C Borman	Montgomery, W Va
Joseph E Brodack	St Louis, Mo
Charles G Brasham	Boston, Mass
Charles I Brown	Ann Arbor, Mich
Charles H Brown	Colorado Springs, Colo
Frederic G Bruns	Battle Creek, Mich
William P Bruns	Providence, R I
Charles P Bruns	Chapel Hill, N C



Frank Walton Burge  
 Herbert Arthur Buins  
 Edward Joseph Burbaum  
 William W Cadbury  
 Edward Swazey Calderwood  
 John L. Calenc  
 Russell J Callender  
 Joseph Almarin Capps  
 James Bain Carey  
 Claude E Case  
 Vern Cavinness  
 Roger M Choisser  
 Leo Gregory Christian  
 Laurance James Clark  
 Frank Clair Clifford  
 Gerald M Chne  
 Peter A Colberg  
 Dean Baldwin Cole  
 George Howell Coleman  
 Mandred W Comfort  
 Edward Franklin Foster Copp  
 George W Covey  
 Sylvester D Craig  
 Walter Stanley Curtis  
 Harold S Davidson  
 Foster L Dennis  
 William Devitt  
 Goodwin A Distler  
 Robert Kenneth Dixon  
 Harold G F Edwards  
 Orville Edward Egbert  
 John Eiman  
 Lewis W Elias  
 Charles A Elliott  
 Harry Smith Emery  
 Edward J Engberg  
 Harvey Milligan Ewing  
 James A Evans  
 Samuel Maurice Femberg  
 Reuben Finkelstein  
 Philip W Flagge  
 Benjamin B Foster  
 Maurice Fremont-Smith  
 Nelson Gopen  
 Edwin L Gardner  
 A Morris Gmsberg  
 Alfred Goldman  
 Alfred Meyer Goltman  
 Edward Victor Goltz  
 Adrian H Grigg  
 Samuel Faitoute Hames  
 George W Hall

Philadelphia, Pa  
 Ah-Gwah-Chung, Minn  
 New York, N Y  
 Canton, China  
 Boston, Mass  
 Aberdeen, S D  
 Tucson, Ariz  
 Chicago, Ill  
 Minneapolis, Minn  
 Clifton Springs, N Y  
 Raleigh, N C  
 Washington, D C  
 Lansing, Mich  
 Vicksburg, Miss  
 Toledo, Ohio  
 Bloomington, Ill  
 Worcester, Mass  
 Richmond, Va  
 Chicago, Ill  
 Rochester, Minn  
 La Jolla, Calif  
 Lincoln, Nebr  
 Winston-Salem, N C  
 Boston, Mass  
 Atlantic City, N J  
 Dodge City, Kansas  
 Allenwood, Pa  
 Woodhaven, L I, N Y  
 Rochester, Minn  
 Shreveport, La  
 El Paso, Texas  
 Philadelphia, Pa  
 Asheville, N C  
 Chicago, Ill  
 Portland, Maine  
 St Paul, Minn  
 Newark, N J  
 La Crosse, Wis  
 Chicago, Ill  
 Brooklyn, N Y  
 High Point, N C  
 Portland, Maine  
 Boston, Mass  
 Washington, D C  
 Minneapolis, Minn  
 Kansas City, Mo  
 St Louis, Mo  
 Memphis, Tenn  
 St Paul, Minn  
 Beckley, W Va  
 Rochester, Minn  
 Chicago, Ill

J Edward Harbinson  
 Charles Lydon Harrell  
 Francis Edward Harrington  
 DeForest R Hastings  
 Harold S Hatch  
 Harry Malcombe Hedge  
 Will Delafield Hereford  
 Edgar Thomas Herrmann  
 George H Hess  
 Frank C Hodges  
 Frederic William Holcomb  
 Charles Edwin Homan, Jr  
 Bayard Taylor Horton  
 James W Hunter, Jr  
 Howard M Jamieson  
 Sydney E Johnson  
 Walter Royle Johnson  
 Sara Murray Jordan  
 Gordon Richard Kamman  
 Elijah Kaplan  
 Karl E Kassowitz  
 Bayard G Keeney  
 Ernest Ellsworth Keet  
 William John Kerr  
 Ray William Kissane  
 Thurman D Kitchen  
 John R Klevia  
 Louis Leon Klostermyer  
 David Nathaniel Kremer  
 George H Lathrope  
 Shuler Upton Lawton  
 William Harry Leake  
 William Mathias LeFevre  
 David Stanley Likely  
 Salvatore Lojcono  
 Chancel Ray Lounsberry  
 Tom Lowry  
 Arthur I Mahrle  
 Fergus O Mahony  
 Thomas Meriwether Marks  
 William Mason  
 Peter Milton Mattill  
 Edgar Mayer  
 Laurence H Mayers  
 William Sharp McCann  
 Daniel Michael McCarthy  
 Donald McCarthy  
 Harry B McCurkle  
 Louis F McGuire  
 Neil C McTernan  
 George Alton Merrill  
 Joseph E Miller

Woodland, Calif  
 Norfolk, Va  
 Minneapolis, Minn  
 Minneapolis, Minn  
 Indianapolis, Ind  
 Chicago, Ill  
 Huntington, W Va  
 St Paul, Minn  
 Uniontown, Pa  
 Huntington, W Va  
 Kingston, N Y  
 Chattanooga, Tenn  
 Rochester, Minn  
 Norfolk, Va  
 Decatur, Ill  
 Louisville, Ky  
 Rochester, Minn  
 Boston, Mass  
 St Paul, Minn  
 New Castle, Pa  
 Milwaukee, Wis  
 Shelbyville, Ind  
 Jamaica, N Y  
 San Francisco, Calif  
 Columbus, Ohio  
 Wake Forest, N C  
 Omaha, Nebr  
 Warsaw, N Y  
 Philadelphia, Pa  
 Newark, N J  
 New York, N Y  
 Los Angeles, Calif  
 Muskegon, Mich  
 New York, N Y  
 Marquette, Mich  
 San Diego, Calif  
 Oklahoma City, Okla  
 Chicago, Ill  
 El Dorado, Ark  
 Lexington, Ky  
 Fall River, Mass  
 Oak Terrace, Minn  
 Saranac Lake, N Y  
 Chicago, Ill  
 Rochester, N Y  
 Brooklyn, N Y  
 Minneapolis, Minn  
 Colorado Springs, Colo  
 Trenton, N J  
 Port au Prince, Haiti  
 Brooklyn, N Y  
 Chicago, Ill

F Clifton Moor  
 John William Moore  
 Garnett Nelson  
 Delbert Harry Nickson  
 Johannes M Nielsen  
 Lillian L Nye  
 Paul A O'Leary  
 Charles C Orr  
 Moses Paulson  
 Warren F Pearce  
 Joseph Maxime Perrot  
 Johannes F Pessel  
 Hugo O Peterson  
 Russell C Pigford  
 Carlos A Pons  
 William Branch Porter  
 Sidney A Portis  
 Ellen Culver Potter  
 Benjamin Harrison Ragle  
 George W Ramsey  
 Hans Reese  
 William Duncan Reid  
 Eugen G Reinartz  
 Wyman Richardson  
 Lester D Riggs  
 Paul Henry Ringer  
 Henry Lawrence Robertson  
 James E Robinson  
 Howard Root  
 A H Ross  
 John Carroll Ruddock  
 Leo Victor Schneider  
 Roscoe Lloyd Sensenich  
 James B Sidbury  
 Clarence E Simonds  
 Harry M Simpson  
 Dwight L Sisco  
 Sidney A Slater  
 Harry LeRoy Smith  
 Henry T Smith  
 Munford Smith  
 Sam Harrison Snider  
 Mary McIndo Spears  
 Oliver H Stansfield  
 Charles William Stevenson  
 Arthur George Sullivan  
 Mary Frances Sweet  
 Ralph M Tandowsky  
 John C Thompson  
 Samuel E Thompson  
 John Thurston Thornton  
 Charles Henry Turkington

Tallahassee, Fla  
 Charleston, W Va  
 Richmond, Va  
 Seattle, Wash  
 Battle Creek, Mich  
 St Paul, Minn  
 Rochester, Minn  
 Asheville, N C  
 Baltimore, Md  
 Quincy, Ill  
 New Orleans, La  
 Trenton, N J  
 Worcester, Mass  
 Tusa, Okla  
 Asbury Park, N J  
 Richmond, Va  
 Chicago, Ill  
 Trenton, N J  
 Boston, Mass  
 Washington, Pa  
 Madison, Wis  
 Boston, Mass  
 Dayton, Ohio  
 Boston, Mass  
 Rutland Heights, Mass  
 Asheville, N C  
 Charleston, W Va  
 Temple, Texas  
 Brookline, Mass  
 Eugene, Oregon  
 Los Angeles, Calif  
 State Sanatorium, Md  
 South Bend, Ind  
 Wilmington, N C  
 Willimantic, Conn  
 Florence, Ala  
 Boston, Mass  
 Worthington, Minn  
 Rochester, Minn  
 McGehee, Ark  
 Boston, Mass  
 Kansas City, Mo  
 Philadelphia, Pa  
 Worcester, Mass  
 Wichita Falls, Texas  
 Hot Springs National Park, Ark  
 Decatur, Ga  
 Salt Lake City, Utah  
 Lincoln, Nebr  
 Kerrville, Texas  
 Wheeling, W Va  
 Litchfield, Conn

Warren Taylor Vaughan  
 Italo Frederick Volini  
 Henry S. Wagner  
 Mortimer Warren  
 Earl C. Waterbury  
 Charles Edward Watts  
 William Frederick Wegge  
 James Fisher Weir  
 Sumner Merrill Wells, Jr.  
 Oliver Clarence Wenger  
 Joel Jesse White  
 Paul Dudley White  
 Harrison A. Wigton  
 Otis Wildman  
 Sidney Dean Wilgus  
 Fred Wooten Wilkerson  
 Robert A. C. Wollenberg  
 George Barrow Worthington  
 George A. Pemberton Wright  
 John G. Young  
 John Peter Zohlen

Richmond, Va  
 Chicago, Ill  
 Pocasset, Mass  
 Portland, Maine  
 Newburgh, N. Y.  
 Seattle, Wash  
 Milwaukee, Wis  
 Rochester, Minn  
 Grand Rapids, Mich  
 Hot Springs National Park, Ark  
 Washington, D. C.  
 Boston, Mass  
 Omaha, Nebr  
 Washington, D. C.  
 Rockford, Ill  
 Montgomery, Ala  
 Detroit, Mich  
 San Diego, Calif  
 Kingston, Jamaica, B. W. I.  
 Dallas, Texas  
 Sheboygan, Wis

The following physicians were duly elected to Associateship at the Minneapolis Clinical Session on February 11

Samuel Simon Mtschuler  
 Arnold S. Anderson  
 Henry B. Bibler  
 Harold Vincent Bickmore  
 James Raymond Boyd  
 Archibald Evans Cardle  
 Austin Clifford Davis  
 David Barden Davis  
 Harold Foster Dunlap  
 Abram Wilbur Duryce  
 Jacob Feigenbaum  
 Lynd Palmer K. Fenger  
 Ralph Lee Fisher  
 Seymour Fiske  
 Wetherbee Fort  
 Thomas Albert Foster  
 Victor K. Funk  
 Francis Joseph Geraghty  
 Samuel Goldberg  
 Julius Gotthelb  
 William Randolph Graham  
 Michael Robert Huley  
 Leon Ralph Hamel  
 John Richard Hamilton  
 Saul Harris, Jr.  
 Albert E. Heit  
 Arthur M. Hoffman  
 Jacob Goldstein  
 Walter Lee Fox

Ann Arbor, Mich  
 Minneapolis, Minn  
 Muncie, Ind  
 Portland, Maine  
 Brooklyn, N. Y.  
 Minneapolis, Minn  
 Rochester, Minn  
 Grand Rapids, Mich  
 Rochester, Minn  
 New York, N. Y.  
 Ann Arbor, Mich  
 Oak Terrace, Minn  
 Detroit, Mich  
 New York, N. Y.  
 Baltimore, Md  
 Portland, Maine  
 Oak Terrace, Minn  
 Baltimore, Md  
 Philadelphia, Pa  
 Lewiston, Maine  
 Richmond, Va  
 Dayton, Ohio  
 Portland, Maine  
 Nassawadox, Va  
 Birmingham, Ala  
 New Rochelle, N. Y.  
 Los Angeles, Calif  
 St. Paul, Minn  
 Los Angeles, Calif

Edgar Webb Loomis  
Earle E Mack  
Robert C Maddox  
Henry M Margolis  
Alexis T Mays  
Ralph J McMahon  
Philip Marsden McNeill  
George LeRoy Merkert  
Edwin Curtis Miller  
Frank B Morrissey  
Gilbert Seymour Osincup  
Wallace Taylor Partch  
Charles Kenneth Petter  
John J Pink  
Rudolph Virchow Powell  
Alfred Hazen Price  
Wallace E Prugh  
D Schuyler Pulford  
Luney Varnon Ragsdale  
Samuel S Riven  
Floyd Leslie Rogers  
Frank E Sayers  
Frances H Schlitz  
Earl Oriol Gregor Schmitt  
Edward William Schoenheit  
Robert James Snider  
Benjamin Bruce Souster  
F C Svoboda  
Walter Clifford Swann  
Edwin Chester Swift  
Joseph Gerard Terrence  
Harold G Trimble  
Henry Hubert Turner  
Silas Willard Wallace  
Ernest S Wegner  
William F Williams  
Harry Hulst Wilson  
Irving Sherwood Wright

Dallas, Texas  
Syracuse, N Y  
Rome, Ga  
Rochester, Minn  
Brooklyn, N Y  
Union, N Y  
Oklahoma City, Okla  
Minneapolis, Minn  
Worcester, Mass  
St Paul, Minn  
Orlando, Fla  
Rochester, Minn  
Oak Terrace, Minn  
Milwaukee, Wis  
St Louis, Mo  
Detroit, Mich  
Dayton, Ohio  
Woodland, Calif  
Bessemer, Ala  
Ann Arbor, Mich  
Lincoln, Nebr  
Terre Haute, Ind  
Wichita, Kansas  
San Jose, Calif  
Asheville, N C  
Wheeling, W Va  
St Paul, Minn  
San Diego, Calif  
Huntington, W Va  
Jacksonville, Fla  
Brooklyn, N Y  
Oakland, Calif  
Oklahoma City, Okla  
Grosse Pointe, Mich  
Lincoln, Nebr  
Cumberland, Md  
Los Angeles, Calif  
New York, N Y

THE AMERICAN COLLEGE OF PHYSICIANS  
FINANCIAL STATEMENTS  
for 1929

Summarizing the Financial Reports, which follow, it may be stated that gross income for the year ending December 31, 1929, amounted to \$68,946 83, and that the net expenditures amounted to \$47,584 44, leaving a balance of \$21,362 39, \$1,200 of which is added to the Endowment Fund and \$20,162 39 added to the principal of the General Fund. During the year, the Endowment Fund, made up of Life Membership subscriptions, was increased from \$4,100 to \$5,300, and the General Fund increased from \$40,461 68 to \$60,624 07, making the total assets of the College as of December 31, 1929, \$65,924 07.

The cost of conducting the Boston Clinical Session was \$9,784 57, which was reduced through profits on the Commercial Exhibits, guest fees and a small Banquet balance by \$6,119 64, or a net of \$3,664 93.

The Annals of Internal Medicine for the calendar year showed a gross cost of \$17,902 46 and a gross income of \$17,073 75, or a net deficit of \$828 71, a great improvement over any previous year in the history of the Journal. The net advertising profit in the Journal was \$2,263 46, which, together with the increased subscriptions, is responsible for the material reduction in the deficit for the Journal.

The following statements have been verified and audited completely by Mr. J. J. Sutton, Auditor.

E. R. LOWLAND, Executive Secretary  
C. R. JONIS, M.D., Treasurer

AMERICAN COLLEGE OF PHYSICIANS, INC  
BALANCE SHEET, DECEMBER 31, 1929  
ASSETS

Cash in Bank and on Hand	\$11,072 62
Bonds Owned, (Schedule No. I)	26,820 60
Accrued Interest on Bonds	524 79
Inventory of Keys, Frames, Pledges, Etc	563 60
	<hr/>
	\$68,981 61
Deferred Expenses for the Fourteenth Annual Clinical Session (Paid in Advance for 1930)	\$ 403 11
Furniture and Equipment	\$ 3,154 80
Less, Allowance for Depreciation	509 00
	<hr/>
Total Assets	\$71,910 52

LIABILITIES

Deposits by Candidates, Applications Pending	\$ 1,570 00
Deferred Income	
Fourteenth Annual Clinical Session Advance Collections for Exhibits	\$ 3,872 35
Annals of Internal Medicine	
Advance Subscriptions, Volume IV	562 10
Advance Subscriptions, Volume V	12 00
	<hr/>
Total Liabilities	6,016 45
Excess of Assets Over Liabilities	<hr/>
	\$65,924 07

FUNDS

Endowment Fund (See Schedule No. II)	\$ 5,300 00
General Fund (See Schedule No. III)	60,624 07
	<hr/>
	\$65,924 07

## SCHEDULE No I

## INVESTMENTS

DECEMBER 31, 1929

<i>Par Values</i>		<i>Cost</i>
\$ 1 000	City of Montreal 5s, 1956	\$ 1,071 30
500	Oklahoma Gas & Electric Co 6s, 1940	487 50
5,000	Province of Ontario 4½s, 1933	4,925 79
1,000	Province of Ontario 5s, 1942	1,052 26
3,000	Steelton, Penna, Paving 4½s, 1933	3,071 25
1,000	Township of Cheltenham, Montgomery Co, Penna, 4½s, 1943	1,000 00
10,000	City of Philadelphia 4½s, 1979	10,225 00
5,000	Canadian National Railway 5s, 40 Year Guarant- eed Bonds 1969	4,987 50
		<hr/>
		\$26,820 60

## SCHEDULE No II

## ENDOWMENT FUND, PRINCIPAL

FOR THE YEAR ENDED DECEMBER 31, 1929

Balance, January 1, 1929	\$ 4,100 00
Life Membership Fees Collected During the Year Ended December 31, 1929	1,200 00
	<hr/>
Balance, December 31, 1929	\$ 5,300 00

## SCHEDULE No III

## GENERAL FUND, PRINCIPAL

FOR THE YEAR ENDED DECEMBER 31, 1929

Balance, January 1, 1929	\$40,461 68
Net Income for the Year Ended December 31, 1929 (Schedule No IV)	20,162 39
	<hr/>
	\$60,624 07

## SCHEDULE No IV

## GENERAL FUND, INCOME AND EXPENSES

FOR THE YEAR ENDED DECEMBER 31, 1929

## INCOME

Annual Dues	\$22,883 00
Initiation Fees	18,765 00
Interest on Bank Deposits	1,373 67
Income from Bonds Owned	743 68
Income from Endowment Fund	282 00
Profit from Sales of Keys, Pledges, Frames, etc	437 64
Receipts from 1927-28 Year Book and Supplement	9 50
Receipts from Annals of Clinical Medicine	58 95

Total Income

\$44,553 44

## EXPENSES

## Thirteenth Annual Clinical Session

## Expenses

Salaries	\$ 3,237 43
Communications	329 83
Stationery and Office Supplies	115 21
Printing	1,471 77
Traveling Expenses	1,963 71
Honorarium	50 00
Entertainment	987 20
Advertising	179 15
Reporting	378 65
Publicity	250 00
Budgets	205 00
Miscellaneous	316 32
	<hr/> \$ 9,784 57

## Deduct

Exhibits	\$ 1,079 49
Guest Fees	988 00
Banquet	152 15
	<hr/> 6,119 64

Net Expenses

\$ 3,664 93

\$ 3,893 97
727 04
13,107 80
40 00
133 05
<hr/> \$17,102 86



## Deduct

## Subscriptions

Volume I	\$ 117 40	
Volume II	560 27	
Volume III	14,131 55	\$14,809 22

## Advertising

Volume II	\$ 1,301 74	
Volume III	951 72	2,263 46

## Stationery and Office Supplies

1 07 \$17 073 75

## Net Expenses

\$ 828 71

## Forward

\$ 4 493 64 \$44 553 44

*Executive Secretary's Office*

## Expenses

Salaries	\$ 7,653 34	
Communications	913 88	
Stationery and Office Supplies	661 99	
Printing	1,622 47	
Rent and Maintenance	3 119 74	
Traveling Expenses	1,599 34	
Annual Audit	350 00	
Miscellaneous	154 92	\$16,075 68

*Treasurer's Office*

## Expenses

Salaries	\$ 360 00	
Communications	20 00	
Stationery and Office Supplies	12 00	
Traveling Expenses	53 00	
Annual Audit	125 00	
Premium on Surety Bond	125 00	
Miscellaneous	15 00	710 00

Annals of Internal Medicine Distributed Free to Life Members

54 00

1929-1930 Directory (Cost of Production and Distribution)

2,714 27

Depreciation on Furniture and Equipment

308 31

Loss on Equipment Traded in

35 15 \$24 391 05

Net Income for the Year, General Fund

\$20,162 39

## OBITUARY

In the death of Dr Lawience Litchfield, on January 16, 1930, western Pennsylvania has lost one of its outstanding figures in Internal Medicine, a loss which will also be felt by the profession generally and by the various medical organizations to whose deliberations he has for long been an esteemed and valued contributor

As a Fellow of the American College of Physicians since 1922 and Governor for the State of Pennsylvania, he has contributed a great deal to the work of the College

A short time ago Dr Litchfield, who had been in failing health for several years, retired from practice. This was made the occasion for a testimonial dinner by approximately 150 friends who gathered to do him honor on the evening of December 6, 1929, at the Pittsburgh Athletic Association. He was presented with a handsome silver memento by the toastmaster, Dr Edward B. Heckel. Among the speakers were Dr William S. Thayer, of Baltimore, Md., and Dr William S. Sharpless, of West Chester, Pa., President of the Pennsylvania State Medical Society.

At the time of his death of coronary thrombosis, he was living at the home of a relative in Chestnut Hill, Philadelphia.

Dr Litchfield was born in Grand Rapids, Mich., a son of General Alvin Cushing Litchfield and Susan Cornelia Carver, a descendant from Robert Carver and William White of Plymouth.

He was a graduate of Harvard University and the Harvard Medical

School, from which he graduated in 1885, and the Bellevue Hospital Medical College of New York University.

Dr Litchfield married Ethel Herr Jones of Pittsburgh in 1898. He traveled extensively in Austria and Vienna and other European medical centers, and was the author of numerous theses on medicine. During the war, he served as Commander Major in the Red Cross and was Chief of Medical Service at Camp Lee, Virginia, and at Camp Grant, Illinois.

He was a practicing physician in Pittsburgh since 1889. Dr Litchfield was staff physician at the West Penn Hospital, Pittsburgh Hospital and Pittsburgh Hospital for Children, and Consultant at the Pittsburgh Eye and Ear Hospital, St John's Hospital and St Joseph's Hospital.

Dr Litchfield was former President of the Pennsylvania Medical Society, and was a member of the Association of American Physicians and former President of the Pittsburgh Academy of Medicine, Allegheny Medical Society, and the College of Physicians of Pittsburgh. He was a member of the executive committee of the International Tuberculosis Congress in 1908 and the International Congress of Hygiene and Demography in 1910.

Besides his wife, he leaves two daughters, Baroness Van Boetzelaer (Ethel Carver Litchfield) and Margaret Litchfield, and a son, Thomas, a sister, Mrs Myra French, of Ripley, N. Y., and a brother, Lucius Carver Litchfield, New York City.

—Submitted by E Bosworth McCready, Governor for western Pennsylvania

Dr Samuel K Pfaltzgraff, (Associate), York, Pa, died November 22, 1929, of coronary thrombosis, aged 65

Dr Pfaltzgraff received his medical degree from the University of Maryland School of Medicine and College of Physicians and Surgeons in 1886. He had been Dermatologist to the York Hospital since 1920. He was an ex-President of his county medical society, a member of the Pennsylvania State Medical Association, a member of the American Medical Association and an Associate of the American College of Physicians since 1923

Dr Burt Wilbur Carr, (Fellow), Washington, D C, died January 13, 1930, of cerebral hemorrhage, aged 54

Dr Carr graduated from the Dartmouth Medical School in 1900. He was in general practice from 1900 until 1918. He became a Captain in the Medical Corps of the U S Army during October, 1918, and then Surgeon in the Reserve Corps of the U S Public Health Service from 1919 to 1922, at which time he was detailed to the U S Veterans' Bureau. He served in the Medical Service as Chief, Occupational Therapy and Physiotherapy Sub-Division, as well as Editor of the U S Veterans' Bureau Medical Bulletin

Dr Carr was a member of the American Medical Association, the New Hampshire Medical Society, the Association of Military Surgeons of the United States and had been a

Fellow of the American College of Physicians since 1928

Dr Harold Cedric Bean (Fellow), Portland, Oregon, was born in Oregon in 1889. He received his bachelor's degree at the University of Oregon and his M D at Johns Hopkins University in 1916. His death on January 1, 1930, was a shock to the profession and his friends for he had been unusually well up to December 25, when he was operated upon for an ulcer in the lower third of the duodenum. A former operation had left many adhesions and localized peritonitis developed.

He was prominent in medical activities in Portland and in the state. He was a member of the State Board of Health and Assistant Professor of Medicine in the University of Oregon Medical School. He had achieved unusual prominence in his chosen field and was beloved by his colleagues.

—Furnished by T Homer Coffen, M D, Governor, Portland, Oregon

Lucius L. Button (Fellow), Rochester, New York, died December 30, 1929. Dr Button was born in Norwich, Connecticut September 11, 1869. He graduated from Sheffield Scientific School Yale University, Ph B, in 1892, from New York Homeopathic Medical College and Hospital, M D, 1895.

He then came to Rochester as an intern at the Rochester Homeopathic Hospital for two years and since that time had been engaged in his practice in this city. During all of these years he occupied various positions on the staff of the Rochester Homeopathic

Hospital, at present the Genesee Hospital, and served several years as an Attending Physician. For the last few years he had been a Consulting Physician at the hospital. For thirty years he had been a special examiner, employed by the Health Bureau, of backward, deficient, incorrigible and truant children.

He was a member of the following societies:

Monroe County Medical Society  
 New York State Medical Society  
 American Medical Association  
 Rochester Academy of Medicine  
 Monroe County Homeopathic Medical Society

Western New York Homeopathic Medical Society

American Association for the Study of the Feeble Minded

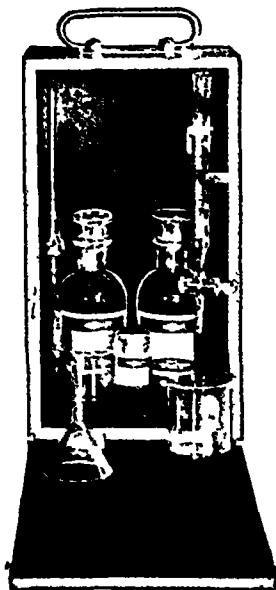
Association for the Study of Infantile Mortality

He was elected to the Fellowship of the American College of Physicians February 25, 1920.

Dr. Button was held in the greatest esteem by his colleagues and was especially beloved by his patients. He presented in his life the best type of the family physician.

—Furnished by David B. Jewett, M.D., Rochester, N. Y.

# "I agree, they're very convenient"



## The LaMotte Blood Urea Outfit

This practical LaMotte Outfit embodies the method of P. S. Hench, M. D., and Martha Aldrich, B. A., (Vol. 38 Archives of Int. Med., Oct., 1926) for the study of urea retention (urea nitrogen by factor).

It is based upon the mercury combining power of the blood, which is an accurate index of the retention of nitrogen and especially of urea. The result is read off directly in milligrams of urea per 100 cc. of blood from the special LaMotte Urea Burette supplied with the set. No calculations are necessary. Results are quantitative.

Readings are easily made with accuracy of 4 mg. of urea per 100 cc. of blood. Only 15 or 20 minutes are required to make a complete estimation. The technic is extremely simple and employs only standard equipment included in each set.

Complete with instructions  
\$18.50—F. O. B. Baltimore

## Other LaMotte Outfits

Blood Sugar	Blood pH (Acidity and Alkalinity)
Urine Sugar	Phenolsulfonphthalein Outfit
Blood Urea	Van den Bergh
Blood Chlorides	Bilirubin Test
Cholesterol	Blood Calcium-Phosphorus
Icterus Index	Hemoglobin
Blood Creatinine	Urine pH (Acidity and Alkalinity)
Blood Uric Acid	
Gastric Acidity	
Blood Bromides	
Complete Urinalysis	



## Users are unanimous in their approval of LaMotte Blood Chemistry Outfits

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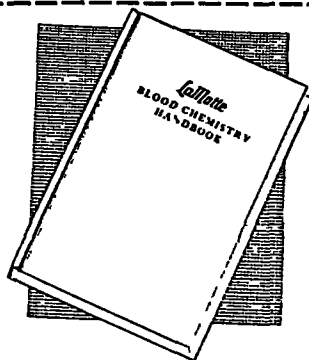
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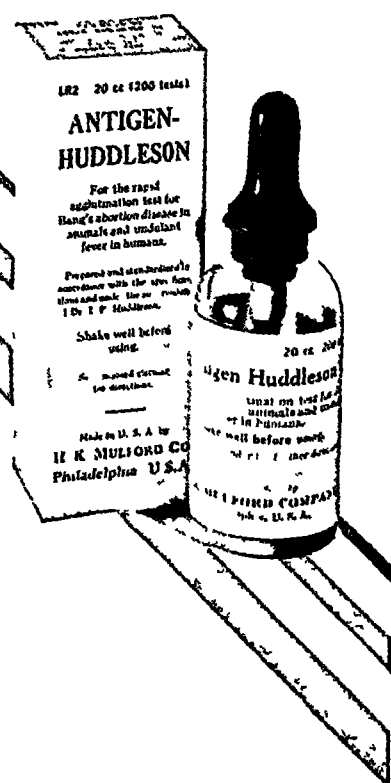
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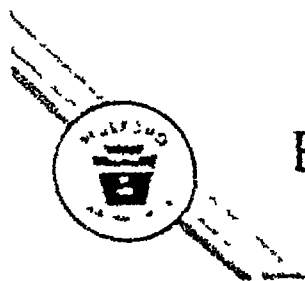
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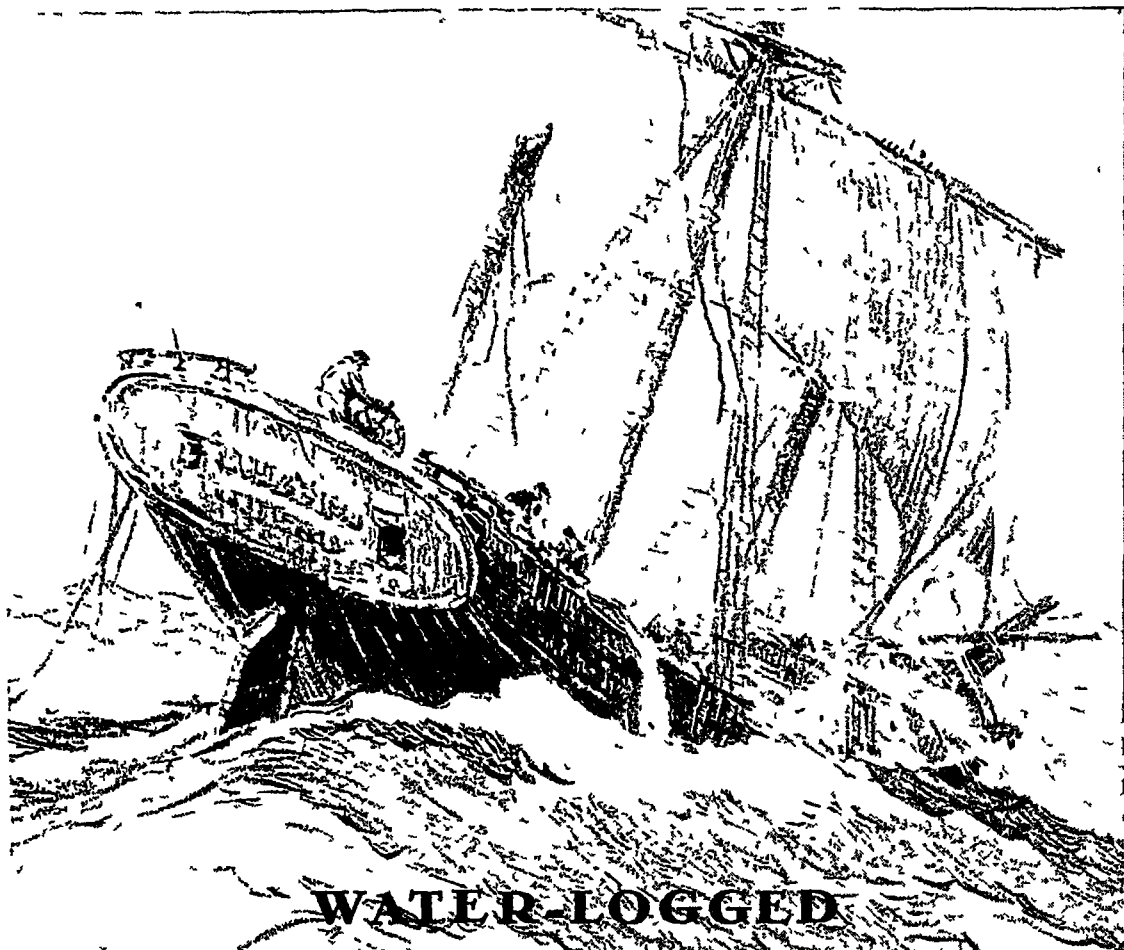
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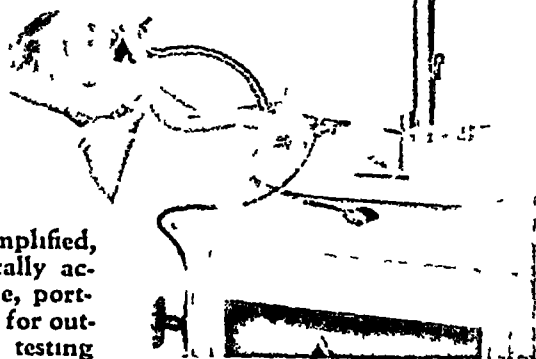
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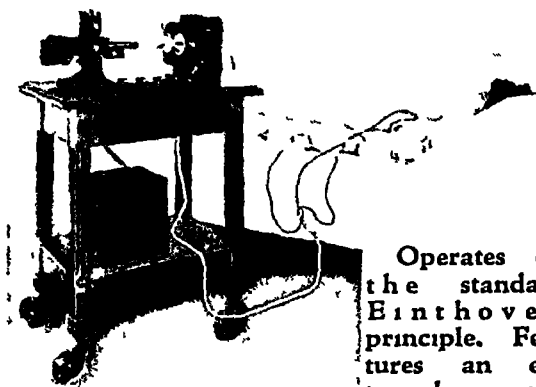
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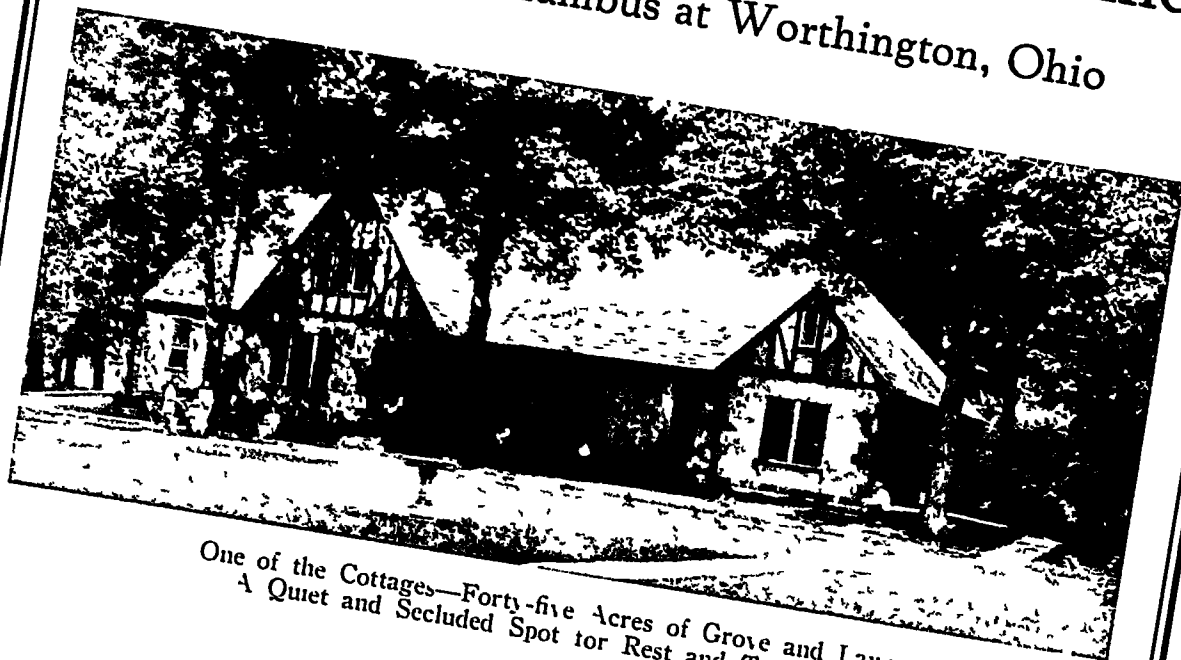
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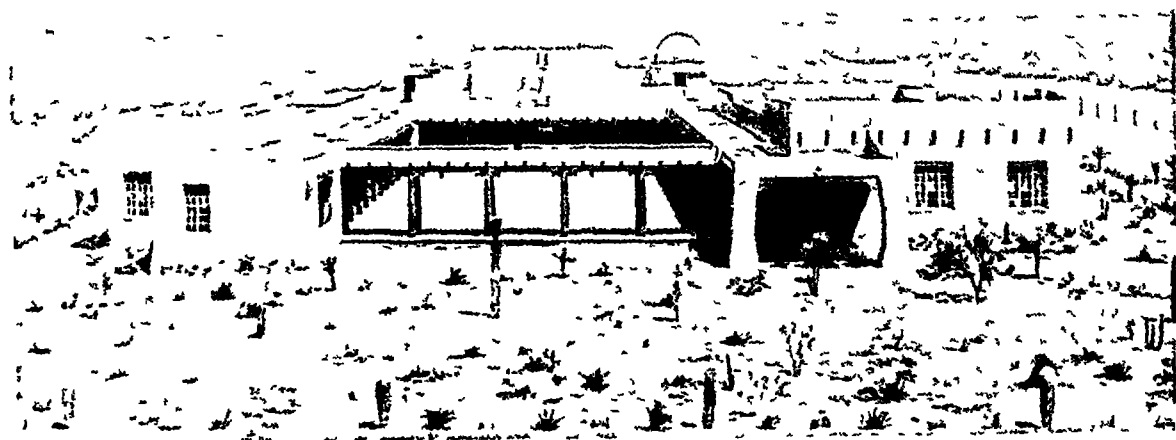
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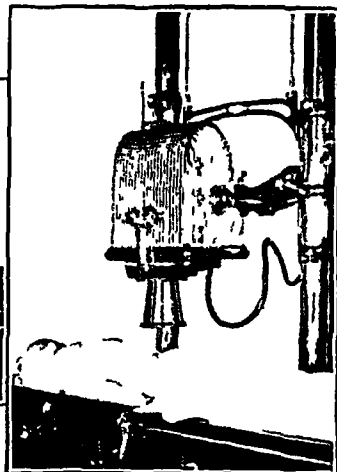
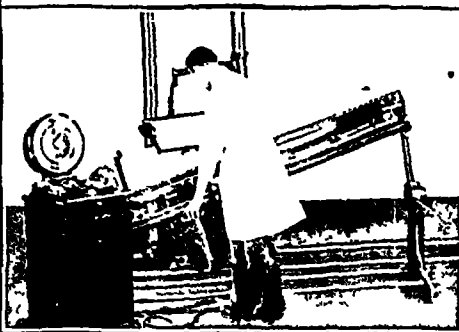
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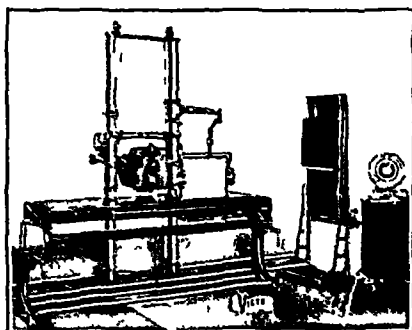
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# The Influence of Venous Filling on the Heart

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## INTRODUCTION

THE functional capacity of the heart is a subject of importance from the purely physiological standpoint. Originally, a short contractile tube as in the perivisceral cavity of an ascidian, it is neither structurally nor functionally much entangled with the creature's other organs. But in higher types in which this simple tube is replaced by closed arterial and venous systems ramifying in every organ, we find that the circulatory apparatus has become structurally interwoven with the whole body. And it has become unable properly to fulfill its office without the help of offices that are quite separated from its own, and unless all of its parts act coordinately, each adequately fulfilling its own distinct and special function.

But the subject assumes practical and commanding significance from the clinical standpoint. The efficiency of the vasomotor system, the nervous system and the condition of the other organs of the body all affect the adequacy of the heart's action. These factors are variable, closely related to each other and create the difficulties in the clinical application of any test for the functional capacity of the heart.

The physiological basis for these, however, has remained in many instances an unturned soil. During the past years, I have carried out some

experiments with the hope of perceiving some light on the physiological basis for some of these tests.

Most of the tests of heart function are based upon the circulatory changes produced by muscular exertion. The clinical symptoms and physical signs may indicate the direction, but probably not the exact level of cardiac efficiency. Changes of pulse rate and blood pressure reveal important criteria in the study of heart function. The technical methods, the sphygmograph, the electrocardiograph and the Roentgen ray have proven themselves valuable adjuvants.

A more or less complete analysis of heart function, particularly from its clinical aspect, therefore, would comprise the following studies:<sup>1</sup>

- I Significant physical signs and symptoms
- II Blood pressure studies and the estimation of the absolute amount of work done by the heart
- III Cardiovascular response to a general demand for increased circulation
  - i Methods depending upon variations in pulse rate
    - a The effect of change of posture upon the pulse rate
    - b The effect of exercise on the pulse rate

- 2 Methods depending upon variations in blood pressure
  - a The effect of change of posture upon the blood-pressure
  - b The effect of exercise upon the blood pressure
  - c The effect of increasing arterial resistance on the blood pressure
- IV Tests of efficiency of the right side of the heart
  - V The polygraph
  - VI The electrocardiograph
  - VII The Roentgen ray and orthocardiograph
    - 1 The variations in the size of the heart during and after work
- VIII Metabolic changes in impaired heart function
  - 1 Vital capacity of the lungs in relation to heart function
  - 2 The elimination of salt as an index of heart function

of the heart's action. The first two factors are very variable.

It is the aim of functional diagnosis to estimate the functional integrity of the heart as a pump, to learn if the heart may submit to the usual demands of active life, and if it can undergo an anticipated amount of strain, such as is entailed by exercise, anesthesia, child-birth, febrile toxemia, etc.

Functional diagnosis should also serve as a clinical index of the increase or diminution of the heart's efficiency with the course of time.

In a comprehensive study of the heart's efficiency, therefore, it should be our aim to ascertain which of the various portions of the cardiovascular mechanism are intact and which are deranged, to what extent the derangement of structure and function affects the circulation of the blood, and to what degree it affects the normal activity and longevity of the individual.

The complementary action of the vasomotor system is very important in maintaining adequate circulation. This factor is different in different individuals and its variations are perhaps the greatest source of error in determining the efficiency of the heart.

From the combined study of the functional organization by means of clinical observation and the use of various technical methods, a fair estimate may be obtained of the functional capacity of the heart.

Perfect functioning of the heart would imply a state in which all the qualities of the cardiac structure are normal and coordinate. In no organ is exemplified to a higher degree the fact that the mutual dependence of functions is proportionate to their



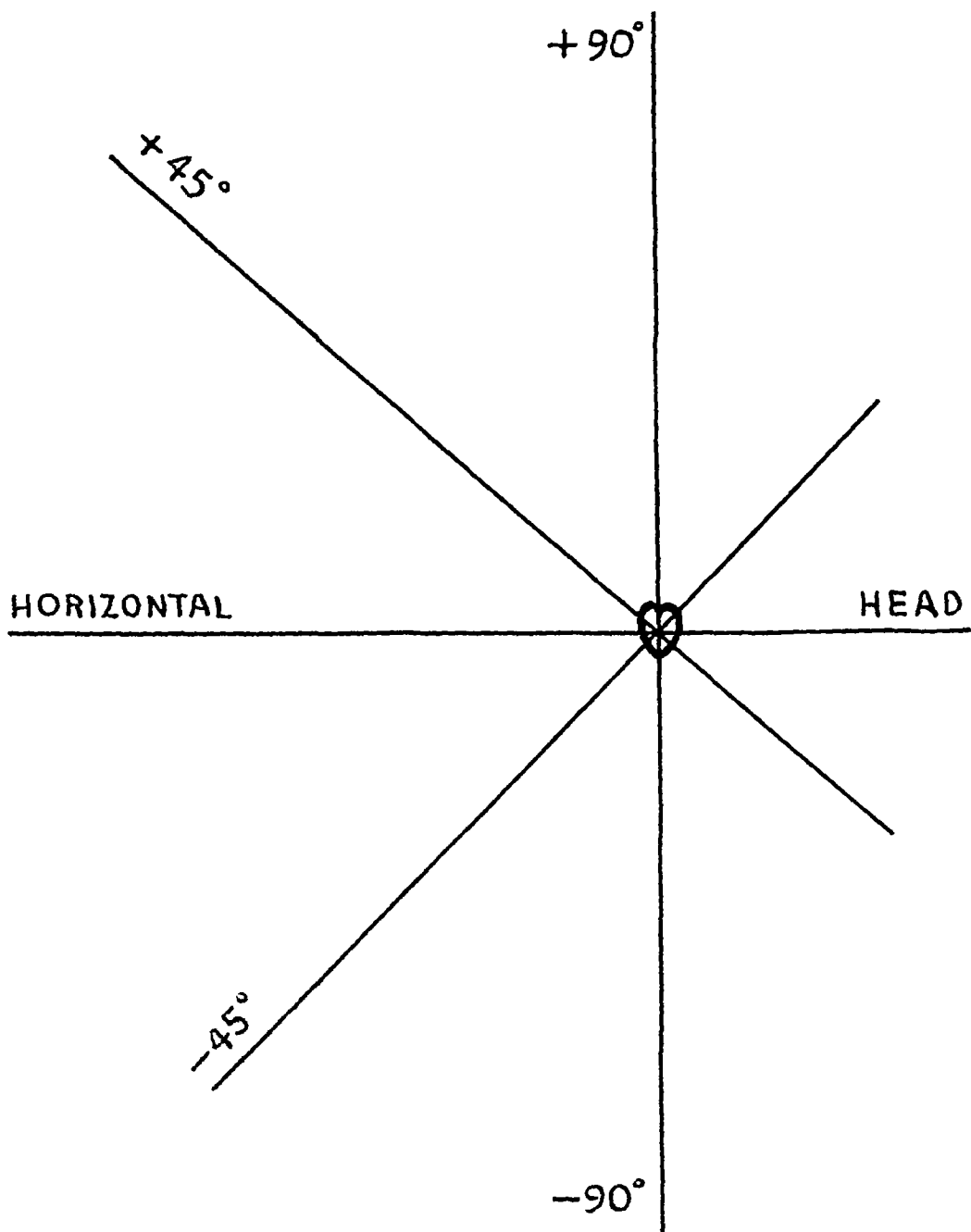


Fig. 2a. Changes in posture effected in the experiments by pivotal

period and then  $-45$  and  $-90$  degrees below the level and a continuous tracing taken during all these procedures. The experiment was repeated several times. (Fig. 2a)



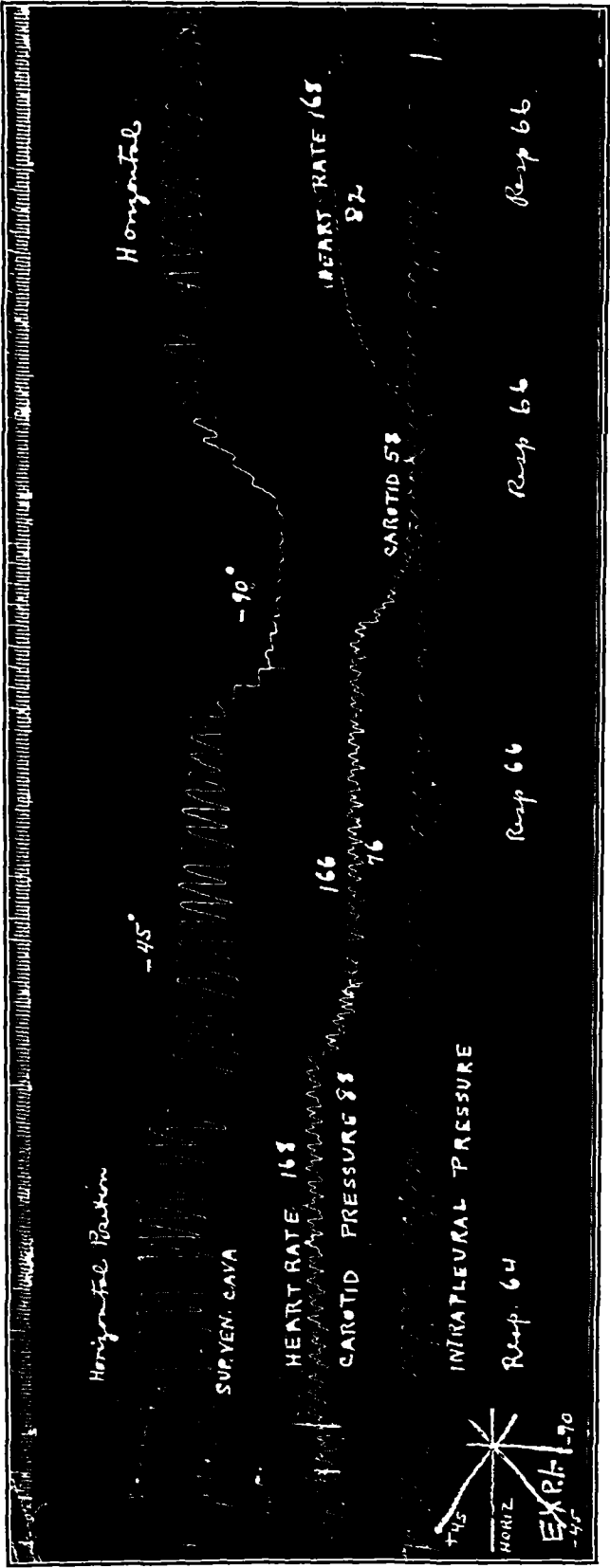


FIG 2a Influence of change of posture on the central venous pressure, on the intracarotid pressure and on the heart rate

### SUMMARY OF RESULTS

1 Change of posture with relation to the heart increasing the central venous pressure produced increase of the heart rate but no characteristic effect on the respiration rate

2 Change of posture with relation to the heart changed the intra-carotid pressure characteristically, an elevation of the main field of the circulation above the level of the heart raised the intra-carotid pressure, and a lowering below the heart level diminished it

3 Parallel effects are seen in the changes in the central venous pressure, i.e., raising the body above the heart level raised, and lowering the body below the heart level lowered the intracaval pressure

4 As in the later experiments, the quickening of the rate of the heart with change of posture was found to be reflex in origin since it no longer occurred after the division of the vagi nerves (Fig. 2b)

### DISCUSSION FROM THE CLINICAL ASPECTS

in elevating the elbow, produces changes in the blood pressure of the arm as the result of both vasomotor and hydrostatic effects upon the column of blood. I showed that the normal effect of raising the arm is a progressive fall of the systolic and diastolic pressure readings as the arm is raised upward, the amount of fall increases with the elevation

We may, therefore, consider the effects of posture on the heart action as parallel with the effects of venous filling or changed venous pressure and shall incorporate and correlate the results of these experiments with those in which injections of isotonic solutions were made.

### THE INFLUENCE OF VENOUS FILLING ON THE HEART RATE

No definite explanation of the ancient observation that the pulse rate in human beings is normally slower in the recumbent than in the erect or semi-erect position was forthcoming until the past decade

Bainbridge<sup>1</sup> experimented with the injection of blood or normal salt solution into the jugular vein in dogs, and came to the following conclusions

1 Increased venous filling of the heart by blood or saline solution leads to a rise of venous pressure and to acceleration and dilatation of the heart, the arterial pressure rises slightly or remains steady

2 The quickening of the rate is reflex in origin since it no longer occurs after division of the vagi and cardiac accelerator nerves

3 It is due chiefly to diminution of vagus tone and partly to increased accelerator tone, there is no evidence

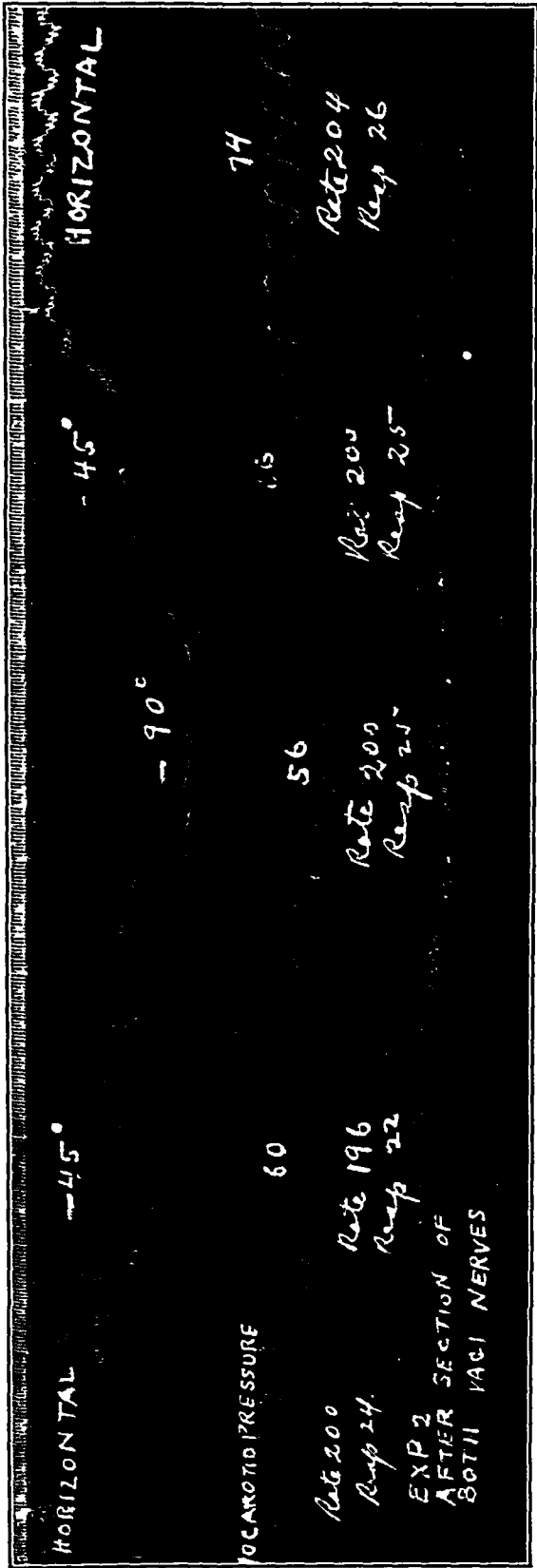


FIG 2b Same after section of both pneumogastric nerves



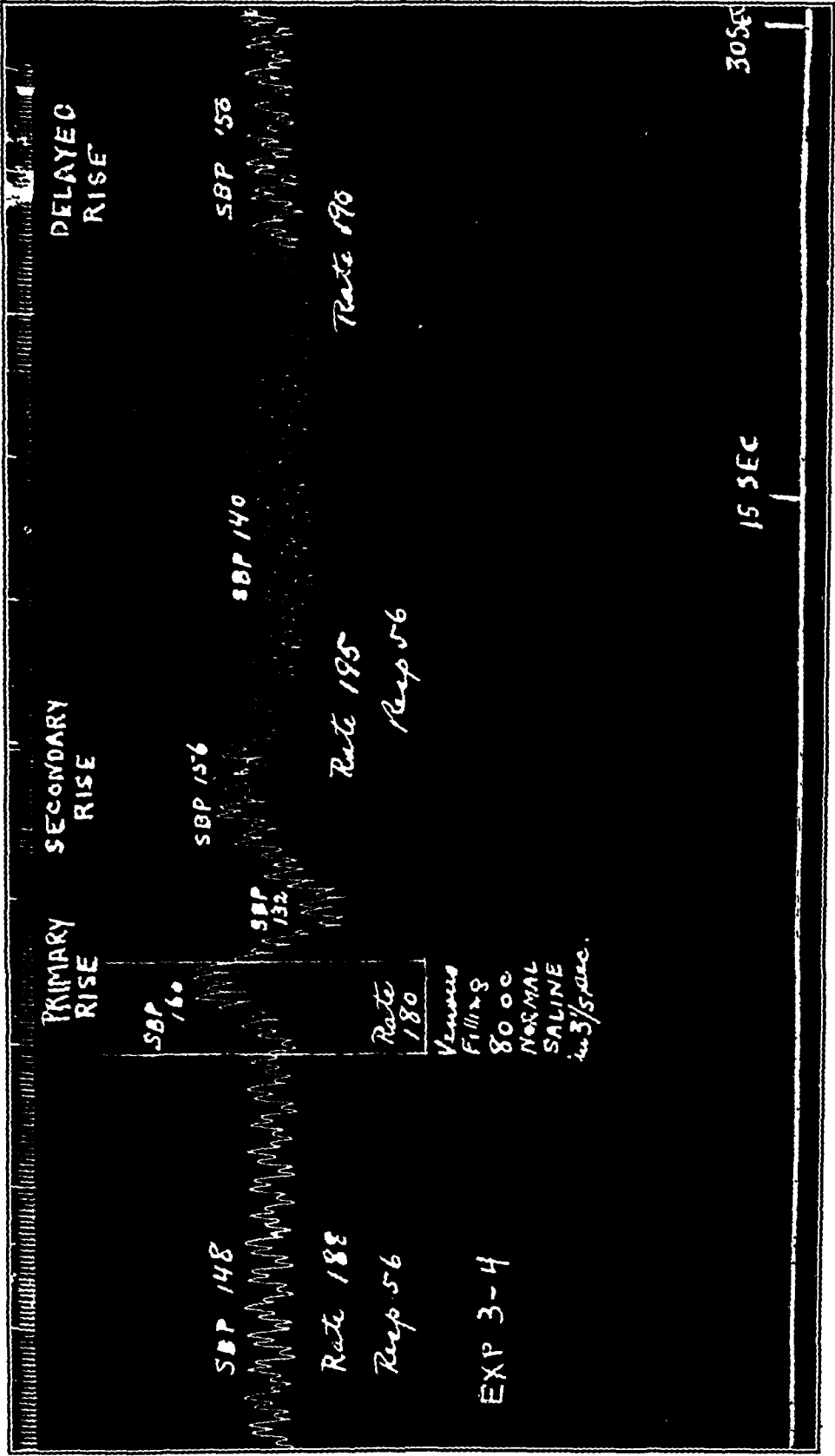


FIG 3 The primary, secondary, and delayed rise of blood pressure following venous filling. Note the fall of the heart rate immediately upon rapid or excessive venous filling.

amount of injected fluid and the rate of injection did distinctly affect the response of the heart

#### DISCUSSION FROM THE CLINICAL ASPECT

As early as 1833, Donnell showed that the pulse rate is normally slower in the recumbent than in the erect or semi-erect position.<sup>8</sup> Schapiro made the observation that the normal difference disappears when the heart is seriously weakened.<sup>9</sup>

Hogersdt and Graupner<sup>10</sup> noted the return of the pulse difference after the effect of digitalis upon the heart was established. In 100 cases recently tested,<sup>11</sup> it was found that the slowing of 7 to 15 beats per minute which recumbency normally produces is diminished or altogether lost in cases of incompetent valvular disease or when the heart is seriously weakened by any cause. Geigel found that a variation of pulse rate above 30 between lying and standing or an inversion of the normal relationship between lying and standing indicates a weakened heart func-

From the postural experiments on dogs, one might question why the heart rate should not increase with recumbency since that position increases the venous filling. The explanation probably lies in the fact that in the erect position, the lessening of aortic tension, as Osborne has shown, causes reflexly a quickening of the rate.

Prevel<sup>14</sup> considers the mechanism causing the acceleration of the pulse on changing from the reclining to the upright position an abdomino-cardiac reflex. The contents of the abdomen slide down, inducing the acceleration of the pulse as the gastric ramifications of the pneumogastric are stretched.

The variations of the pulse rate following exercise were the first to be studied in their functional significance. Mendelsohn and Graupner<sup>15</sup> estimated the length of time it takes for a normal heart to return to its previous rate after a measured amount of work. The time it takes for any given heart to return to normal after a definite amount of exercise was then suggested as a measure of its functional capacity. The longer the time it takes to return to the normal rate, the less efficient the heart is considered.

Mendelsohn asserted it as a principle that, the greater the amount of work done with prompt return to the normal rate, the greater is the functional capacity of the heart. He emphasized the point that the amount of work should be considered as of relative value only. Absolute amounts of work cannot be laid down as the normal for any person because the capacity for work varies with the weight, muscular development and general makeup of the individual.

# INTRINSIC OR VENOUS FILLING ON THE BLOOD PRESSURE

From one standpoint, it may be the-

oretically assumed that the increase in heart rate and the pressure changes that follow venous filling are analogous to those changes that take place after exercise. Aluscular work mechanically increases the amount of blood re-

turning to the heart. Tachycardia, as has been shown, would result in a measure proportionate to the amounts of work performed in a given period. Upon the subsidence of the work, the cardiac intake diminishes and the heart rate promptly falls.

Normally, an increase in systolic pressure takes place simultaneously with the work and in a way this is proportionate to the amount of the work. The pressure rises to its highest point at the end of the exercise, and then promptly falls within a period of two minutes. Upon this principle are based a number of tests of the functional capacity of the heart as evidenced by its reaction after exercise.

From my experiments conducted on this subject, it appears that venous filling is followed by a characteristic form of pressure curve depending upon the amount of solution injected, the time in which it is introduced, and the previous condition of the heart and circulation.

For the convenience of description, the three curves that take place may be called the primary or immediate rise, the secondary rise and the delayed rise (Fig 3).

The injection of a small amount of fluid, such as will apparently not tax the heart, gives rise to an immediate elevation of the carotid pressure fol-

lowed by a prompt, though slightly more gradual fall, to about the previous level. Analyzing the tracings carefully, this fall, in every instance, appears to be slightly below the previous level with a gradual return to the normal within about one minute. When the heart has already been overtaxed by previous injection of solution, or when it has not quite recovered from the previous injection, or when the injected quantity is great, then the form of the curve, although analogous to the one previously described, shows distinct accentuations of the primary rise, a slight fall, a secondary rise, and finally, a fall below normal and a delayed rise. This is characteristically illustrated in figure 3.

When large amounts are injected suddenly into a normal dog's heart the first rise is followed by a slight fall immediately upon the cessation of the venous filling, or in slow injections when a large enough amount has been introduced. This is followed by an immediate rise of short duration and a more gradual fall returning to the normal within a minute. If the blood pressure is, therefore, measured at intervals of 15 seconds following the injection, it will be found that the pressure will rise in the series of readings until about one minute after the injection (Fig 4).

It would thus seem that overwork of the heart muscle stimulated by venous filling occasions, or at least markedly exaggerates, what may be called "a delayed rise of blood pressure."

When, however, the heart has been excessively overfilled and an injection subsequently made, the form of curve,

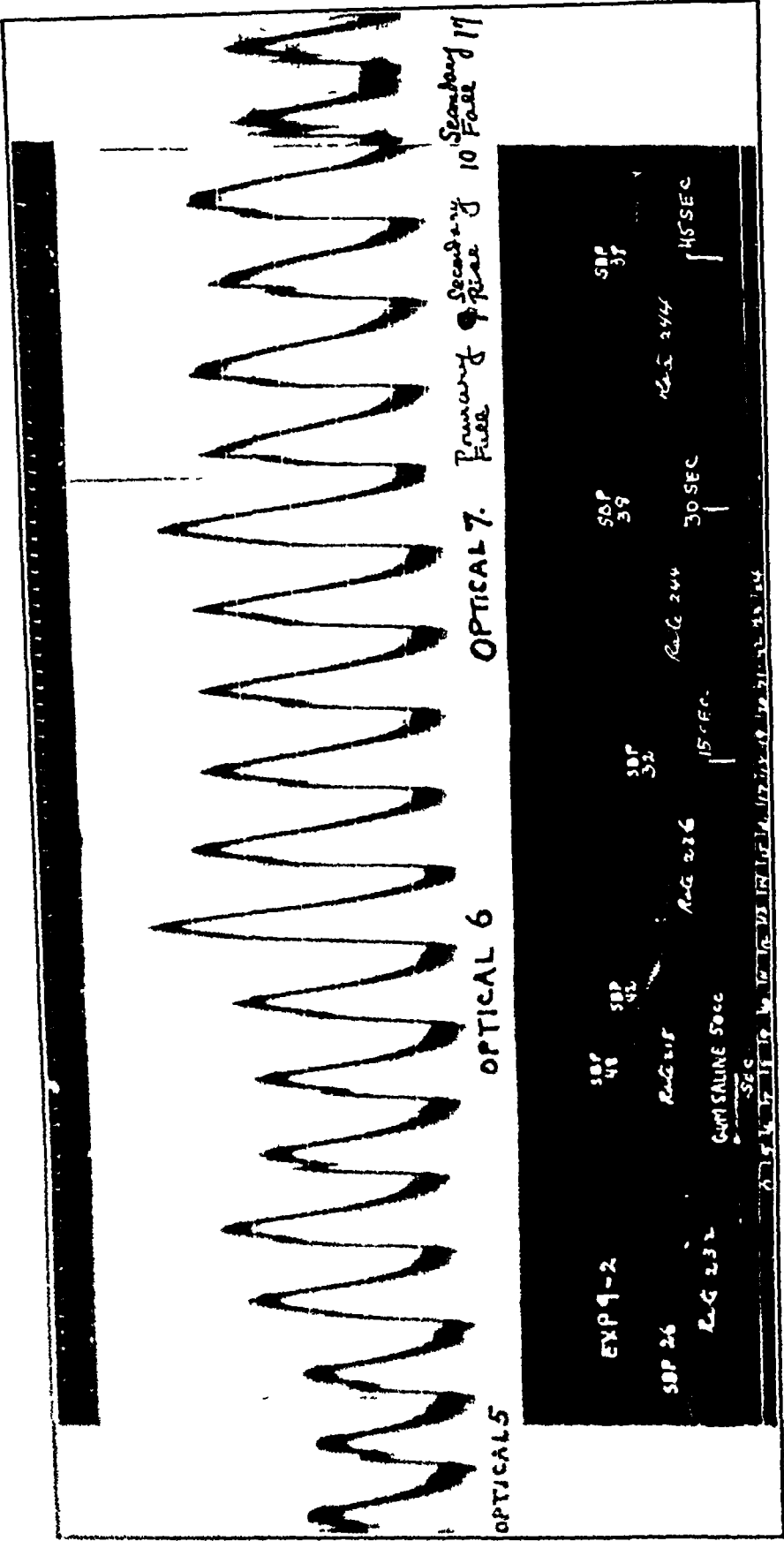


Fig. 4 Blood pressure and intraventricular pressure curves produced by venous filling



although still maintaining the same outline, becomes more level throughout and the changes are not so marked.

It is interesting to note, as can be easily understood, that if the right auricle is distended by means of a balloon there do not occur any marked changes in the arterial pressure.<sup>5</sup>

#### DISCUSSION FROM THE CLINICAL ASPECT

*Graupner's Test*—Graupner's test for estimating the functional capacity of the heart depends upon the principle that the reaction of the weakened heart to a measured amount of work differs from the reaction of the normal heart. In this test a definite amount of work is executed by a group of muscles measured by a Zuntz ergometer, and blood pressure estimations are made before, during and after the work.<sup>16</sup>

Graupner reached the following conclusions:

- 1 A moderate amount of work, in normal hearts, will cause a rise of blood pressure after the work. This either promptly returns to normal or remains constant at the higher level for a period, but does not fluctuate and gradually returns to normal.

- 2 The greater the amount of work done, the higher the rise of blood pressure, and the quicker the return to normal, the more efficient is the myocardium.

- 3 A sinking of the blood-pressure after muscular exertion, declining from the start, or even a very slight rise after work of about ten mm. mercury, which falls again almost immediately to below the original point is evidence of incapacity of that heart for that amount of work.

- 4 If the blood pressure remains high for a period after the work and then suddenly falls, it is evidence of overstrain or fatigue.

- 5 If the blood pressure after work is lower than normal, and then slowly returns to normal but does not rise above normal, a primary myocardial weakness exists. This reaction is characteristic of myocardial insufficiency.

Graupner's test depends upon the fact that the ventricle reacts to muscular work which at first increases the blood pressure. If the ventricle proves unequal to the task of maintaining the pressure, there occurs a compensatory increase in pulse rate but a fall in blood pressure.

*Barringer's Test*—Aino Lehdorff<sup>17</sup> showed experimentally in 1908 that stimulation of the splanchnics produces their contraction with increase of blood pressure to a varying degree. If the heart's action becomes insufficient, however, the blood pressure falls. With the recovery of the heart's contraction the pressure rises again.

Some years ago Barringer described a test of heart function, using Graupner's method of making frequent readings of the pulse rate and systolic blood pressure after a measured amount of work and clinically obtaining Lehdorff's experimental results in insufficiency of the heart.<sup>18</sup>

The theoretical considerations Barringer presented as follows:

Muscular work increases the CO<sub>2</sub> content of the blood. This stimulates the nervous centers controlling the suprarenal glands. An increase in the adrenalin content of the blood is thereby produced, which causes a constriction of the vessels in the splan-

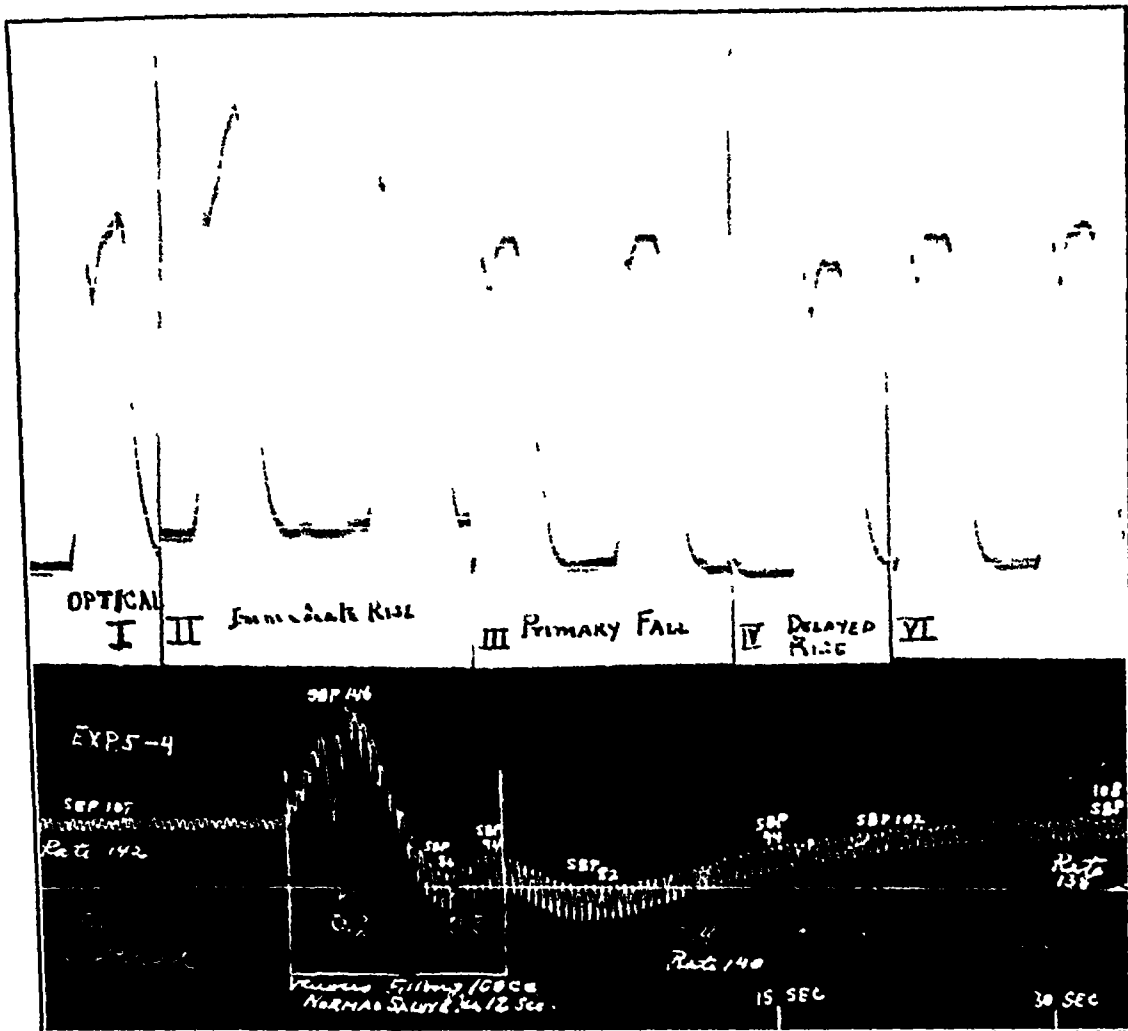


FIG 5 Intraventricular pressure curves produced by venous filling, the curves were made by means of the Franck capsule, each section is numerically indicated by a corresponding signal on the smoked tracing below

Wiggers showed that saline infusion causes a definite prolongation of the ejection phase quite independent of the length of the diastole and that the systolic discharge of the heart may not be regulated by changes in the duration of cycle alone

As the heart accelerates and the cycle shortens, the succeeding diastolic filling is encroached on more and more until the diastolic inflow is abbreviated and systolic discharge is greatly affected. This tendency of the diastolic

filling to be decreased as the heart accelerates is one of the fundamental compensatory mechanisms which prevents an excessive minute volume from being discharged during rapid heart action

As Wiggers has shown the initial pressure increase in the right ventricle was always associated with an increase in initial diastolic volume. When the initial pressure becomes elevated to an excessive degree, the intraventricular pressure-maximum no longer in-

creases but becomes lower at the same time that the systolic discharge lessened. When the heart is long distended by a great inflow its subsequent power of response is reduced. The irritability of the heart may also be depressed or stimulated by chemical agents, in which case the pressure-maximum and systolic discharge are not related to the initial pressure.

When the heart was obviously dilated, neither increased initial pressure nor increased initial length determines the vigor of the ventricle as the myocardium is depressed.

Viewing all the experimental evidence in the light of the more fundamental work of Blix, Hill and others on skeletal muscle, we must be ready to admit that the dynamic efficiency of the ventricle may be fundamentally determined by such factors as initial length, diastolic surface-volume relation, and initial tension.

The ventricles are filled to capacity even under very low auricular pressures. It would seem that any additional increase in volume must necessitate a stretching of the elastic and tonic walls of the ventricle. This requires an increased auricular and increased initial pressure. The pressure required to stretch the walls sufficiently to admit a definite volume increase need not be great, if the tonus is low, but must be considerable if it is high.

The series of tracings from my experiments and the subjoined legends illustrate the changes that take place under the conditions of the experiments (Fig 6).

The effect of venous filling on the intraventricular pressure as evidenced by the tracings obtained by means of

the optical manometer is quite characteristic. As has been shown by Wiggers, any sudden increase in venous filling which increases the volume of the ventricles always promptly elevates the initial tension and pressure-maximum in both ventricles. After the injection of solution there is definite increase in the systolic discharge in a few seconds. Toward the end of the infusion, a further elevation initial or maximum pressure in the ventricles is observed.

When the arterial resistance increases as by mechanical compression of the aorta as was done in one of my experiments, the initial pressure is elevated (Fig 7). This is due to the dilation of the ventricles that it causes, i.e., to increase in the length of the muscle fibers. It is by overdistension of the right heart, due to the high venous pressure, that the heart finally fails.

#### DISCUSSION FROM THE CLINICAL ASPECT

Normally the wave caused by the auricles discharging their contents into the ventricles may be absent from the cardiogram of the apex beat or may present itself as a slight elevation just preceding the systole of the ventricle. The resistance to the auricular current offered by the wall of the ventricle is analogous to that offered by contracted arteries to the systole of the heart.

There are two important conditions which would have the effect of increasing the size of the wave due to auricular systole. (1) Relative hypertrophy of the auricles with increase in the force of their impulse and (2) loss

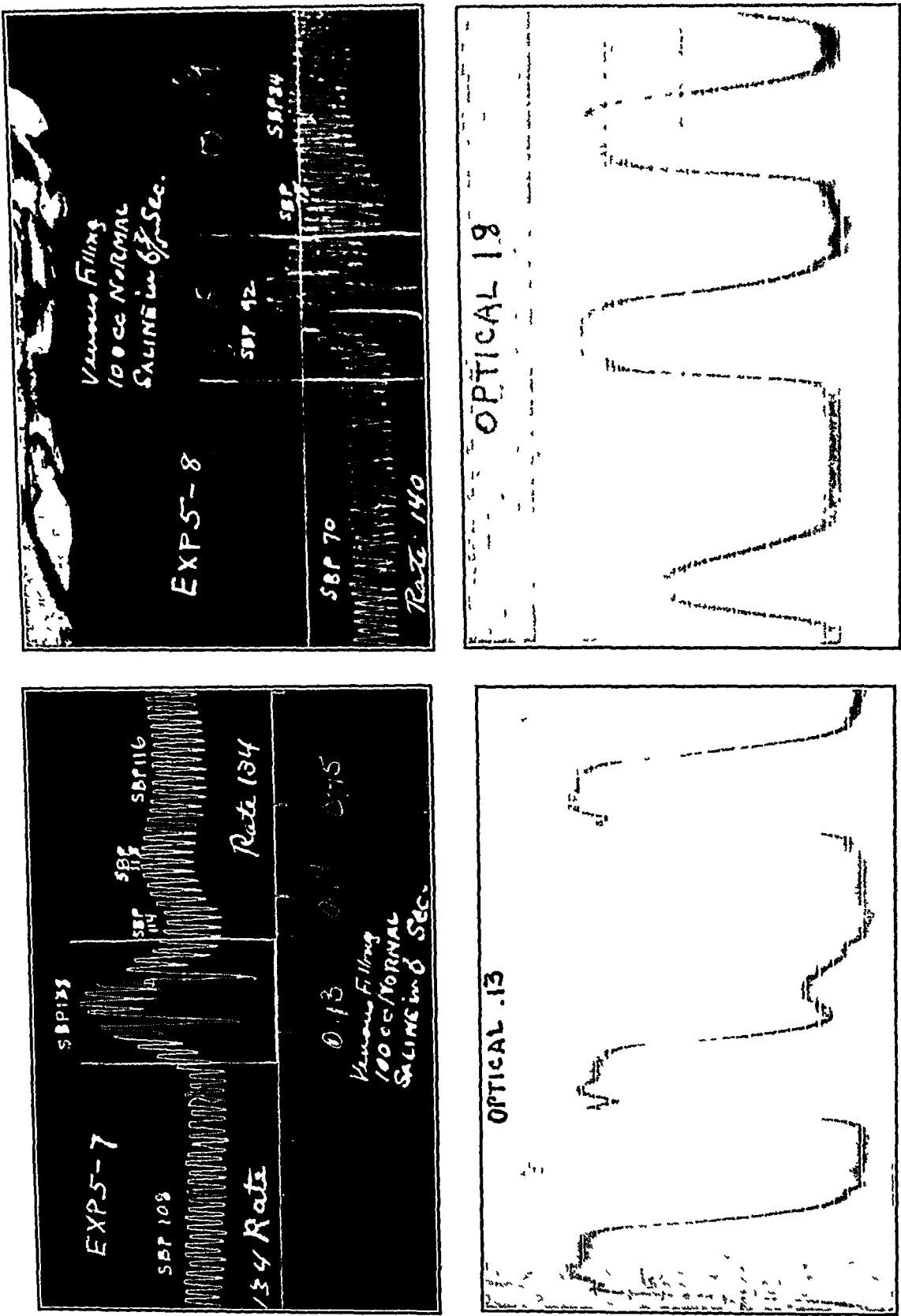


Fig 6 Intraventricular pressure curves during extrasystolic beats, produced by various filling

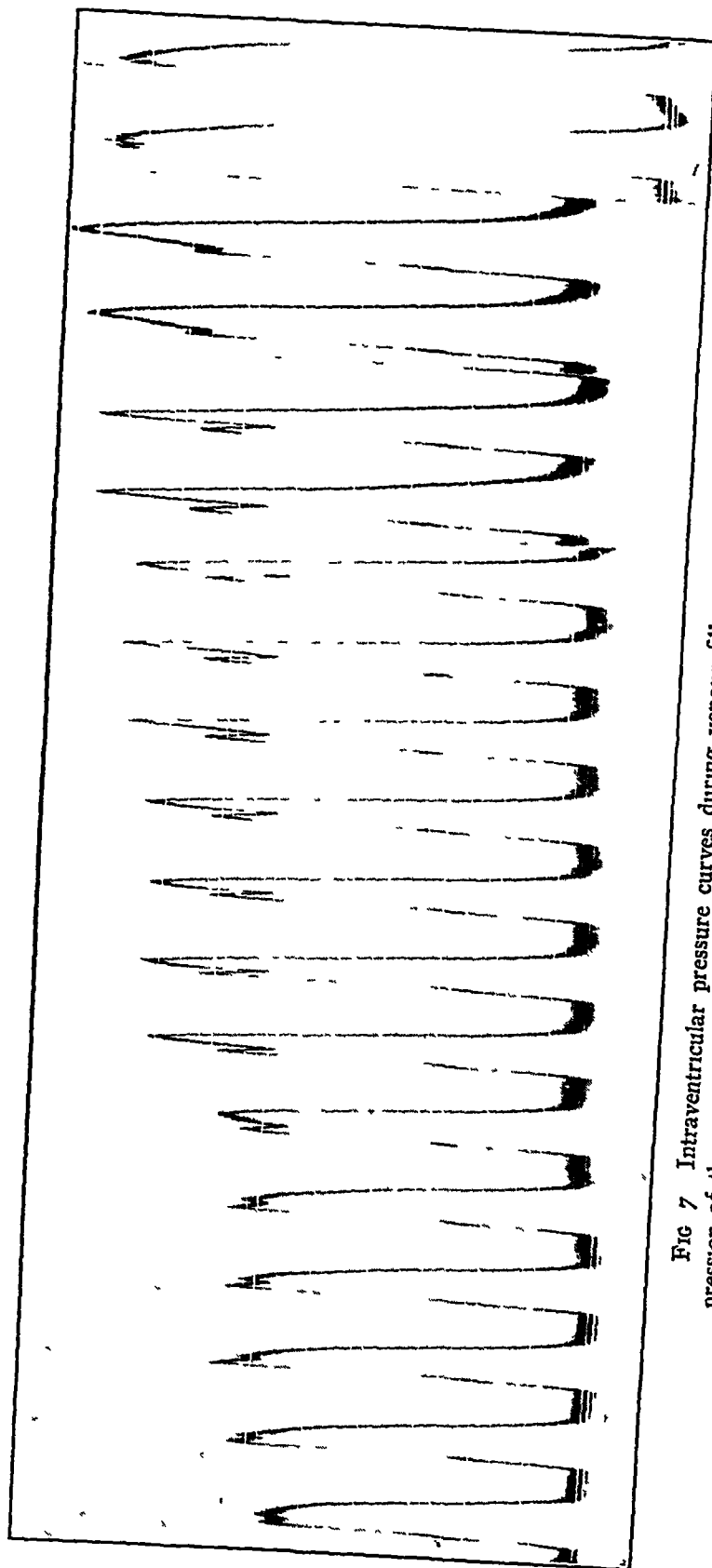


FIG 7 Intraventricular pressure curves during venous filling with simultaneous compression of the aorta, and resulting progressive dilation of the heart

of tonicity of the ventricles with dilation and thinning of their wall

(1) With reference to the wave "a" of the cardiogram in cases of mitral stenosis, it shows itself as a thrill or series of waves at the beginning of systole and not as a distinct single impulse

(2) Loss of tonicity of the ventricular muscle increases the prominence of the "a" wave in the apex curve. In this condition the heart lies markedly dilated against the chest wall. The rise of the "a" wave is abrupt, the curve of filling is steeper than normal.<sup>2</sup>

#### THE INFLUENCE OF VENOUS FILLING ON THE PRODUCTION OF EXTRASYSTOLES

Among the abnormalities of cardiac mechanism induced by venous filling, extrasystoles are particularly frequent. They are apparently of ventricular origin. They occur in most instances only after the heart has been considerably distended by fluid. Their first appearance is usually immediately upon the injection of a large quantity of fluid at the height of the primary rise of blood pressure. They promptly disappear and do not recur if the heart is not further tried. The tracings show plainly that they occur at the time of greatest heart strain, and when the demand upon the heart is greatest for a readjustment of its action. (See fig 6)

#### INFLUENCE OF VENOUS FILLING ON THE HEART VOLUME

Changes in the length of the muscle fibers, as Frank, Patterson, Piper and Starling and others have pointed out, may be evaluated most satisfactorily by studying the changes in the ven-

tricular volume during consecutive phases of the heart cycle

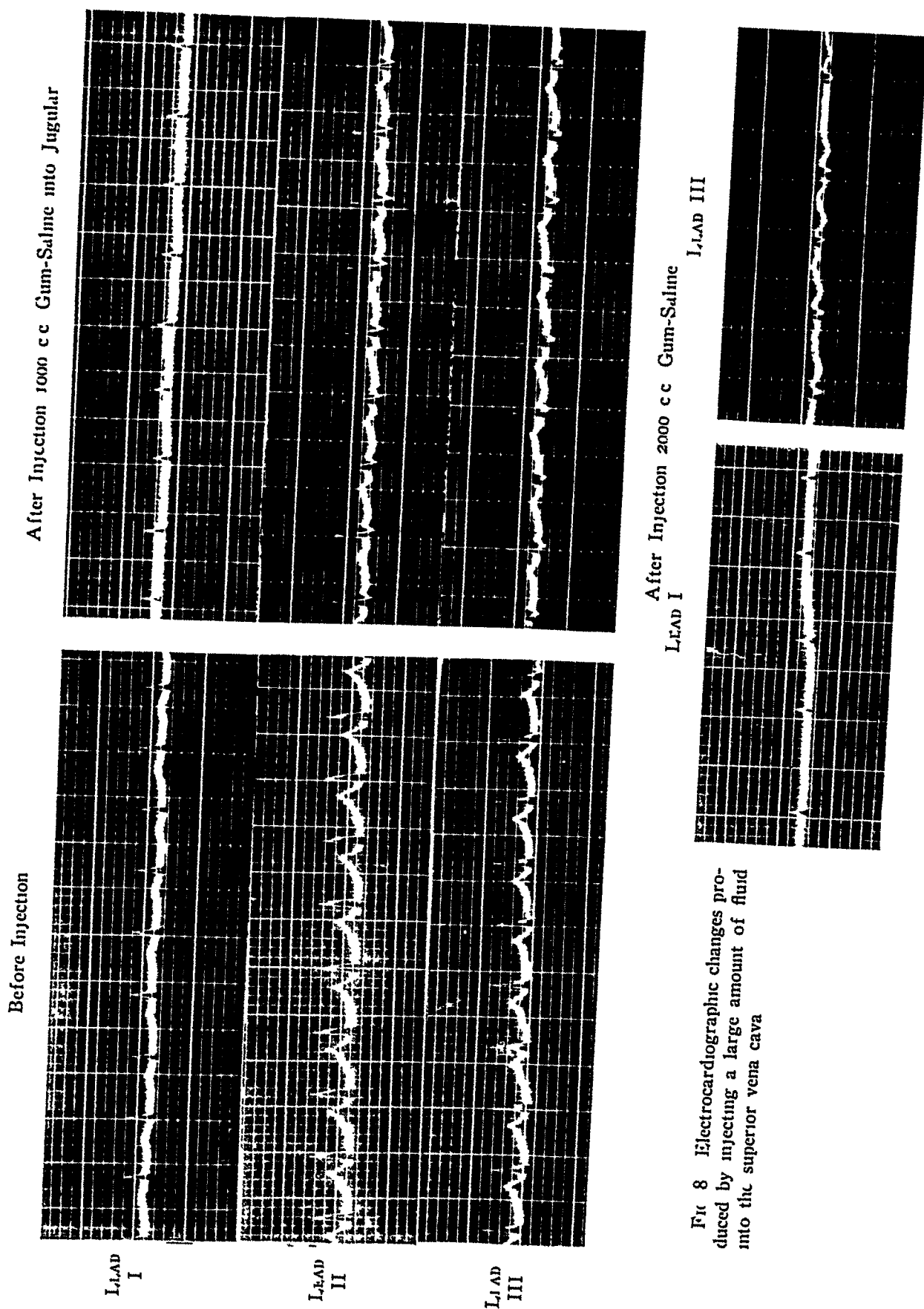
Patterson, Piper and Starling found that when the venous inflow increases, the ventricles are more distended in diastole and the systolic discharge increases. The initial tension in the left ventricle, however, may not increase, but on the contrary may actually be lower. Nevertheless, the intraventricular pressure-maximum appears to rise.

Straub found that when the inflow rate is increased, the two ventricles dilate somewhat and expel larger systolic volume. The intraventricular pressure curves taken from the two ventricles showed differences. In the right ventricle, changes similar to those reported by Wiggers were constantly observed, i.e., increased diastolic filling always occasions an increased initial tension and a higher pressure-maximum. In the left ventricle and in confirmation of Starling's results no changes in initial tension occur although the pressure curves did become somewhat higher. According to these results, the increased discharge of the right ventricle is unable to affect the diastolic filling of the left sufficiently to cause an elevation of initial tension.

The plethysmographic curves taken in my experiment show an increase of the ventricular portion of the heart in its diastolic volume, a diminution in its systolic volume, and therefore an increased intake and output as a result of venous filling (Fig 7)

#### THE INFLUENCE OF VENOUS FILLING ON THE ELECTROCARDIOGRAM

I endeavored in this thesis to ascertain if pure dilatation of the right



ventricle will produce an electrocardiogram indicating right ventricular preponderance

I therefore obtained the three leads of an electrocardiogram from a normal dog. I then injected about 1000 c.c. of gum saline solution through the jugular vein and repeated the electrocardiogram. Continuing the injection during the course of this experiment, I repeated leads I and III and obtained the prints recorded in fig. 8. Analyzing these, it is evident that a striking change was produced in the form of the electrocardiogram by the injection

of a large amount of fluid into the right heart. There is noticeable a distinct suggestion or indication of right predominance.

The particular change noted is a diminution in the voltage in all three leads. Equally important and significant is the alteration in the form of the S-T phase progressively assuming a negative direction with final inversion of the T wave. The clinical interpretation is important. This suggests that inversion of the T wave in lead III is a significant sign of cardiac stress or dilatation.

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# A New Instrument Utilizing Controlled Air Pressure for Dilating Spastic Lesions of the Esophagus (Especially of the Cardia).

By FRANK SMITHIES, M D , Sc D , *Chicago, Ill*

FOR more than ten years there has been no advance suggested in instruments constructed for the purpose of treating esophageal lesions of the "spastic type (esophagismus, spasm at the cardia, cardiospasm)

This report describes a dilator useful, particularly, in the radical local management of cardiospasm associated with diffuse dilation of the esophagus

Commonly, instrumentation for the relief of this syndrome is attempted by the "hydrostatic," elongated balloon described many years ago by Henry Plummer. Excellent though Plummer's apparatus is, it has several faults and limitations. (1) A source of running water is required—such demand limits use of the instrument to a specially arranged office or clinic room, (2) a special adaptor is requisite to connect the dilator with the water supply, (3) the whalebone staff, employed to carry the balloon to the cardia, "shreds" and swells when wet, resulting in its definite weakening, in dirt collection, and, what is most important, so narrowing the lumen of the rubber tube carrying the water about it, as to interfere seriously with controlled filling, emptying and quick removal of the

dilating balloon in emergencies, (4) the large water pressure gauge is unwieldy, expensive and often in the way, (5) adjustment of the silk sac and rubber balloons is difficult, these necessary appendages must be specially shaped and made—a not inconsiderable expense item, moreover, many instrument supply houses do not carry the silk sacs and rubber balloons in stock, much delay in replacement of a damaged part often is experienced

The dilator developed by me, with the technical assistance of Mr Hutchcraft of Sharp & Smith, Chicago, is designed to remedy some of the limitations of Plummer's apparatus. It is a "pneumatic," not a "hydrostatic" dilator. Hence, it is readily portable, requires no special connection to water or air supply, is clean and easily handled, needs only a small pressure gauge, has no whale-bone staff to interfere with rapid and accurate distension and deflation of the dilating balloon, has a double safety control against over-distension and to facilitate rapid deflation of the balloon and quick withdrawal of the instrument in emergencies, its balloons and restraining sac are constructed of material readily available and easily adjusted. The en-

the apparatus can be distributed at a reasonable cost and its several parts are conveniently replaceable. Finally, the length of the guiding staff of the instrument is adequate, whereas practically all the esophageal dilators on the market, whether of the olive or the balloon type, are too short, by many inches, for practical employment.

mer) which is tunnelled so as to permit the introduction of a stout, silk-twist thread as a guide through the narrowed esophagus or cardia. The tip is available in standard sizes. The steel staff is 30 inches long and chromium plated. This increased length over staffs usually sold with "hand-me-down" instruments, is of great prac-

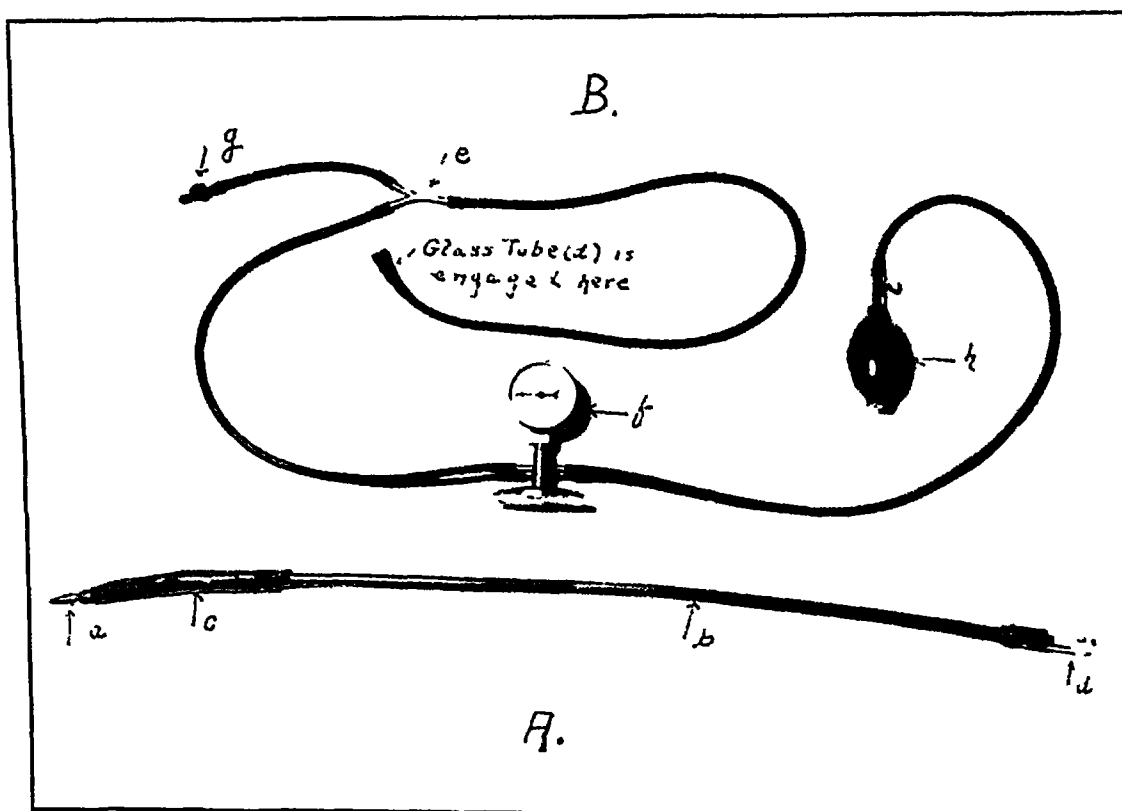


FIG 1—Photographs A and B

Our apparatus conveniently may be described in two sections (a)—the expansile dilator with its staff for introduction and (b)—the mechanism for inducing and controlling an distension of the dilating sacs.

(a) Fig 1 (Photo A)—A steel staff, round in cross section, sufficiently flexible yet strong, carries at its distal tip (a) a bougie of wedge type (Plum-

tical value it permits the dilating sacs actually to engage the cardia, however tall the subject—something not possible with the short-staffed instruments sold over the counters in appliance shops. The distal end of the staff carries a metal spool-tube three fourths inches long and threaded for the reception of the wedge-shaped bougies. This tube also serves to anchor the stout



Fig 1

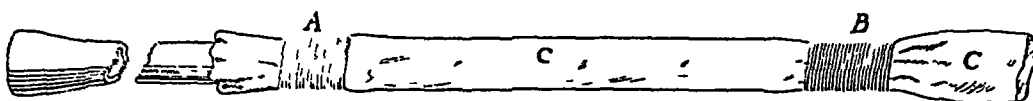


Fig 2

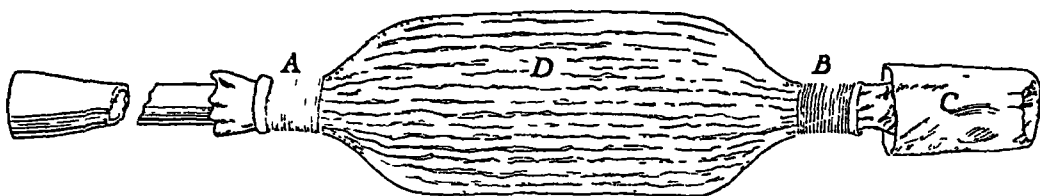


Fig 3



Fig 4

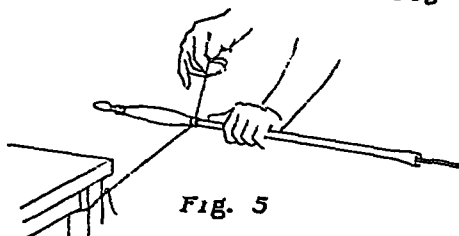


Fig. 5

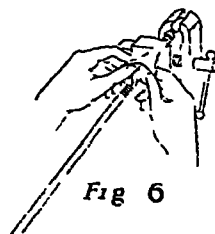


Fig 6

FIG 2—Sketch T

#### SKETCH I Rubber tube with perforations

The details of the expansile section of the apparatus are shown in Fig 2 The mode of adjusting the rubber bags and cloth retaining sacs is as follows

(A) Metal Tube (B) Metal spool tube Over these tubes (A & B) the Penrose tubing and cloth bag are fastened

FIG 2 Penrose tubing (C) fastened and tied over metal tube (A) and metal spool (B)

FIG 3 The cloth bag (D) is slipped over Penrose tubing (C) and tied at (A and B, after which the Penrose tubing is cuffed over the cloth bag (D) and tied off at (A)

FIG 4 Shows the complete dilator bag (F) is a lead washer used to make joint with olive (G) air tight (E) is a round metal staff to facilitate introduction

FIG 5 Showing method of fastening Penrose tubing (C) and cloth bag (D) to the rubber tube

By anchoring one end of the silk the tying of the bag and tubing is most satisfactorily accomplished

FIG 6 The metal staff is placed in rubber tube and the olive attached Same is then held in a vice The Penrose tubing is then grasped with both hands as shown and the tubing is cuffed over the cloth bag (D) and tied at (A)

rubber tubing, (b) perforated in its distal six inches, which encloses the steel staff, serves as an air conduit and receives the rubber and silk dilating bags (c). The rubber tubing has a diameter of  $7/16$  inches and is 29 inches long.

A special feature of the dilating bags is the material of which they are made and the ease with which they may be adjusted. We have attempted to do away with "special" sacs—expensive and difficult to secure—by using stock materials ("Penrose" or ordinary "cigarette" diam rubber tubing). The details of the sacs and the method of placing them in position are as follows:

(b) The air-inflation mechanism (Photo B)—This is joined to the dilating staff by a glass tube (d) 3 inches long and  $3/4$  inch in diameter. Both distal and proximal ends of this glass tube are flanged in order to hold the rubber tubes snugly and prevent slipping and air loss.

From the proximal end of the connecting glass tube, a strong rubber tube, 28 inches in length and  $1/4$  inch in calibre, leads to a metal Y (e). This tubing is made of such length for convenience in handling the dilator when that has been introduced into the oesophagus. From one limb of the Y, a rubber tube 20 inches long passes to a pressure gauge (b) (U.S. Gauge Co.—No. A D—1444) of 15 lbs registering capacity, small, yet adequate

From the second limb of the Y, a rubber tube 6 inches long passes to a hard rubber stop-cock (g). This is a "safety valve" in case, in emergency, rapid deflation of the dilating rubber sacs is desired and should the inflating bulb (h) fail to function. We consider this to be an important feature of the apparatus: its worth will be appreciated by those who have had experience with "hydrostatic" dilators whose whalebone shafts have become swollen by water and thus have prevented quick collapse of the dilating sacs and the prompt removal of the instrument from the esophagus of a distressed patient.

From the pressure gauge a rubber tube, 30 inches long, leads to a standard rubber bulb, of English make, similar to the bulbs used in the best form of blood pressure apparatus. This bulb has one way action, and has the usual screw type deflation valve.

The entire apparatus is quickly assembled, is compact, durable and practical. By actual use, we have found it far superior as a working apparatus, to any form of expansile dilating, esophageal mechanism thus far available. Where one wishes to dilate stenoses under fluoroscopic control, the advantages of this "pneumatic" over the "hydrostatic" type of dilator are obvious. It can be used in X-ray rooms without water attachments, is quick, clean, positive and safe.

# Gastric Manifestations in Constitutional Inadequacy\*

By ARTHUR C. CLARK, M.D., *Kansas City, Mo*

**H**IPPOCRATES was one of the first, who noted that body build and temperament were greatly affected by climatic conditions. He also observed in women a relationship between adiposity, menstrual disturbances, and sterility. In 1840 Addison<sup>1</sup> and Hutchinson<sup>2</sup> wrote descriptions of the types of people, who seem to be susceptible to certain maladies. They thought habitus or physical form of the individual bears an important relationship to disease. DiGiovanni<sup>3</sup> in 1880 developed a plan for anthropometric study of patients. He at first thought that it was the morphology that determined the character of the disease. Bean<sup>4</sup> in 1912 correlated observations on body-form and disease propensity. Diaper<sup>5</sup> in exhaustive investigations classified man according to disease potentialities.

Goldthwait<sup>6</sup> recognized definite anatomic types that were present in chronic disease. He rarely found the normal type in the chronic patient. In his Shattuck lecture he made a plea for careful study of the anatomic type of patient, who was subject to disease. This plea has met only a limited response except for the efforts of a few workers.

In studying human constitution, we consider not only the morphological and functional characteristics but also those hereditary characteristics influenced more or less by environment. We must consider those qualities which are inherent in the germ-plasm and are passed from one generation to another through the physical agency of the chromosomes. Pende<sup>7</sup> defines constitution as a morphological, physiological, and psychological resultant of the properties of the body and of the combination of these in a special cellular state having a balance and functional output of its own, a given capacity for adaptation and a mode of reaction to its environmental stimuli. Julius Bauer<sup>8</sup> says that constitution represents an accumulation of potential energies, containing categories of special type, different from those of morphology and physiology. The primordium in the germ-plasm controlling body stature is a constitutional characteristic which may be noted in families as well as races.

It is our purpose in this paper to present our observations of a series of cases of constitutional imbalance or deficiency in which the chief complaints were symptoms referable to the gastro-intestinal tract. The more complete the balance, co-ordination and unification of body elements, the stronger

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\*Read before the Jackson County Medical Society, Kansas City, Missouri, October 20, 1929

the constitution to exogenous causes. Any excess or deficiency of a part will impair the general dynamic equilibrium, and will represent a reason for constitutional weakness and disease. Viola's<sup>9</sup> studies showed that evolutionary disharmony between the two systems constitutes the primary natural reason for the deviation from the normal. In certain organs certain types of tissue may preponderate or may be deficient causing interstitial tissues to function imperfectly. The term "constitutional inadequacy" describes the physical or psychical imbalance of an individual, causing personal or environmental disharmony. In studying the constitution, we consider the morphological, the physiological, and the psychological aspect.

Under morphology we consider the relationship between the trunk and limbs. The broad type of build is called megalosplanchnic, hypoevolute or herbivorous, the long type of build is called microsplanchnic, hyperevolute or carnivorous. There may be local types out of harmony with general body habitus, such as a preponderance of cardiovascular, digestive, sexual or hemolymphopoietic systems. Clinically the morphological study of the development of each system is essential.

In the pure microsplanchnic, hyperevolute, or longitudinal type, there is a predominance of the thyroid alone, or of the thyroid, pituitary, and adrenal together, although mixed forms may occur, while in the megalosplanchnic there is a hypo-function of the thyroid, or of the thyroid and pituitary together.

Most important is the rôle of the

sympathetic and parasympathetic systems. In sympathicotomia, an indication of constitutional hyperexcitability of the sympathetic system, we have tachycardia, spasm of arterioles, hypertension after emotion, with secretory and motor inhibition of the stomach and colon. In vagotomia or hyperexcitability of the parasympathetic system, we have hypersecretion, salivary, nasal, lachrymal, gastric and intestinal, hyperperistalsis, hyperchlorhydria, vomiting, localized spasm in the stomach and colon, habitual constipation, bradycardia, and hypotension.

The normal type of body has a normal inclination of the pelvis, normal elevation of the ribs, normal position of the shoulders, a torso of moderate length and of moderate breadth, thorax, full, moderately rounded, upper abdomen rounded, lumbar region shows a mild curve forward, the mid-lumbar area, inclination backward. The large bowel is adherent to the post-abdominal wall on the right side up to the region of the liver, turns forward and inward crossing with a slight sag to the splenic flexure up in the left side of the abdomen behind the stomach from which point it is again attached to the peritoneal wall until it reaches the sigmoid. The transverse part of the colon is attached to the liver upon the right side and to the stomach in the center of the body. The stomach and liver are attached to the diaphragm and the suspensory ligament of the diaphragm is the pericardium which is attached to the anterior part of the lower cervical spine. In the upper abdomen, lies the aortic plexus, and the ganglia so placed that when the organs are in their proper

position, there is the least possible pressure on them

In the megalosplanchnic, (Case 1) the stature is medium or below medium, with excess body mass, horizontal diameters greater than longitudinal, large head, premature baldness, face broad or pentagonal, abdomen, larger than trunk, upper abdomen, larger than lower with umbilicus low, skin, tough and oily, stomach, short, horizontal type, large bowel, long and of large caliber. The endocrine system may show an atonic, flaccid type, such as a hypothyroid variety, characterized by vagotonia in which there is a tendency to constipation, migraine, articular pains, asthenia, and somnolence after meals. Individuals are slow in movement and in psychic reaction. The nervous system is sensitive, the individuals are moody, possess a low blood pressure, and have great tolerance for sugar.

Disturbance in posture due to large and heavy viscera causes backward inclination at the hips. Imperfect action of the liver or the formation of gall stones may be influenced by mechanical interference with the structures upon which function depends. Proper mechanistic and anatomic considerations should be given to these abdominal conditions. The inability of the stomach to empty or the variations in character of its secretions may be due to the position of the organ or to disturbance in the nerves or blood vessels.

Microsplanchnics (Case 2) show a tendency toward gastro-intestinal dyspepsias and splanchnoptosis, pernicious anemia, ulcers of the stomach and duodenum, intestinal disorders, tubercu-

losis and nervous disturbances (Case 7). There is a deficiency development of the system that assimilates energy and accelerates metabolism, hence these individuals are thin. The digestive apparatus shows an atonic and ptosed stomach. These individuals possess a voracious appetite, but are unable to put on weight. They have high acid values, good peristalsis, and rapid emptying rate. The stomach is long and tubular, attachments are less firm, and downward displacement is greater when standing. The small bowel is shorter, walls are thinner and lumen smaller. The mesentery is longer and in standing the small bowel lies in the upper pelvis or lower abdomen. The large intestine is shorter and more mobile. On the right side, there is a free mesentery, permitting this portion to change its position easily. The left side has a mesentery so that in the upright position, the entire colon lies below the crest of the ileum. On account of the absence of the retroperitoneal fat the vessels and nerves lying on the spine are constantly irritated, the same with the adrenals, which are unprotected by fat pads, permitting mechanical interference to take place. The loosely attached organs drag backward, and thus in the reclining position they may cause subnormal temperature, low blood pressure, and general lack of vitality. Oftimes the diaphragm is depressed and the abdominal wall is relaxed with lessened support of the wall which forces the organs downward. Careful study of the maladjustments of the parts or study of posture often gives one a clue to correction of pathological changes in the abdomen.

There are two functional types of gastric constitution hyperasthenic and the asthenic. The hyperasthenic stomach is characteristic of the megalosplanchnic. They have a large stomach, large capacity for food, eat slowly due to the tone of the stomach and esophagus. In this type the stomach and esophagus dilate slowly. The asthenic type is characteristic of the microsplanchnic. Due to poor tonus, the stomach is always open, fills easily, hence food passes rapidly. In megalosplanchnics, the amount of secretion is large and in microsplanchnics, diminished, so in megalosplanchnics, large amounts of water are necessary to dilute the gastric juices.

The exact function of the vagus, sympathetic, and intrinsic nervous formations of the stomach relative to tonicity and peristaltic functions are still unknown. Bickle<sup>10</sup> states that the vagus and sympathetic have both stimulating and inhibitory fibers. The vagus acts more on the pyloric sphincter, antrum and pars media, and the sympathetic acts on the fundus and cardia. When the fundus and cardia contract, the other parts relax and vice versa. Eppinger and Hess<sup>11</sup> found in vagotonics, hypertonia of the sphincter and of the pylorus, hence the bull's horn type of stomach, where the stomach fills slowly, producing heart symptoms due to raising of the diaphragm. The sensory disturbances are burning, pain, sense of acidity in the throat, not due to excessive acid but to vagal hyperesthesia of the gastro-esophageal mucosa or to muscle irritability.<sup>12</sup>

Ulcer is prone to occur in the hypertonic area along the lesser curvature, where food irritates it. This part is more spastic hence it favors obstruc-

tion of the small blood vessels. Food also remains longer in the stomach, emptying is slower and acid chyme remains longer in contact with the ischemic mucosa, producing a tendency to ulcer formation. Some types of ulcer must be considered as constitutional, a true trophic neurosis of the gastric or duodenal wall, not the same as a constitutional neurosis of the stomach. Ulcer generally attacks individuals with a weak stomach, who have suffered for years from dyspeptic disturbances, and who have stigmata of hyperirritability of the vagus. These patients often correspond to the asthenic, microsplanchnic type with hyperthyroidism and hyperadrenalism (Case 5).

Relative to the secretory insufficiency, achylia or hypochylia, complete or partial, there is a degenerative stigma occurring often in several members of the same family, often associated with neuropathic diathesis, along with geographic tongue, perverted appetite, constitutional albuminuria, constitutional bradycardia, and various endocrine anomalies, such as hyperthyroidism, goiter, and diabetes. As the cause of secretory anomaly, we find protopathic weakness of the secretory cells, and constitutional vagal hypotonia.

Achylia is often associated with gastric hyperperistalsis, and in the presence of a permanent opening of the pylorus, secondary intestinal disorders, as diarrhea arise. Sometimes states of achylia and hyper-secretion or of hyperchlorhydria alternate in the same subject. This is common in endocrine dyscrasias as hyperthyroidism and hypoparathyroidism. It is probable that a constitutional gastric sympathicotonia predisposes to such secretory changes.



Gastric hypotonia is due to a constitutional sympathicotonia. The preponderant tonus of the sympathetic is associated with a condition of diminished tonic contraction of the pylorus, and hence with a more ready emptying of the stomach.

In megalosplanchnics we have a long, large bowel causing the fecal matter to be dry and fully formed, of importance in habitual constipation. Microsplanchnics have short, small intestines which make only partial use of the alimentary material, so that a part of this is subject to decomposition by the bacterial flora in the large bowel, or to elimination in the form of copious semifluid feces. We often find intestinal disturbances in subjects with exudative lymphatic, neuroarthritic or vagotonic diathesis on account of the extensive, reticulated lymphatic tissue (Case 10). These disturbances are paroxysmal phenomena often resembling anaphylactic crises.

In exudative diathesis occurring in childhood, there are anomalies of metabolism (Case 10). The infantile type is characterized by marked development of connective and lymphatic tissues, by preponderance of tonus of excitatory-anabolic nerves, parasympathetic and vaso-dilators, and preponderance of certain hormones in the endocrine balance such as thymus and pineal over the less-evolved functionally, as pituitary, adrenal, and genital hormones. These patients have urticaria, protein-shock, and anaphylaxis.

Enteroptosis has a deleterious influence upon the respiratory and circulatory system. Lack of support of the diaphragm results in suppression of the diaphragmatic lower costal respi-

ration. Here the auxiliary respiratory muscles, act and lift up the upper half of the thorax, the base being restricted. Intra-abdominal blood not being subjected to the normal inspiratory pressure accumulates in the abdominal viscera, especially in the liver, producing a congestion of the abdominal vessels, hemorrhoids, and renal stasis, and an ischemia of the upper half of the body, with resultant faintness and dizziness.

Certain individuals have the characteristics of the bilious temperament. Familial simple cholemia is a hereditary anomaly of bile production and secretory function of the liver. Here there is a small amount of bilirubin circulating in the blood stream. These individuals are disposed to acquire gall stones, infectious icterus, and primary cancer.

Microsplanchnics of the hyperthyroid, hypoadrenal type, often are descendants of gouty or diabetic individuals. This constitutional hyperbilirubinemia is not due to disturbances of the biliary system, but probably due to insufficient function of hepatic cells, which do not convey all the bile pigments into the bile ducts.

Chauffard<sup>13</sup> assumes an incapacity of the hepatic cell to transform the cholesterol of the blood and to eliminate it in the bile. He found that cholesterinemia, which often is hereditary, is present in individuals of the arthritic family, which very often possess biliary calculi. Cholesterol metabolism is governed by certain endocrine tissues such as adrenal cortex, corpus luteum, interstitial glands, thymus, and anterior-lobe pituitary, therefore it is readily understood why gall bladder cases have a characteristic facies.



FIG 1—Case 1

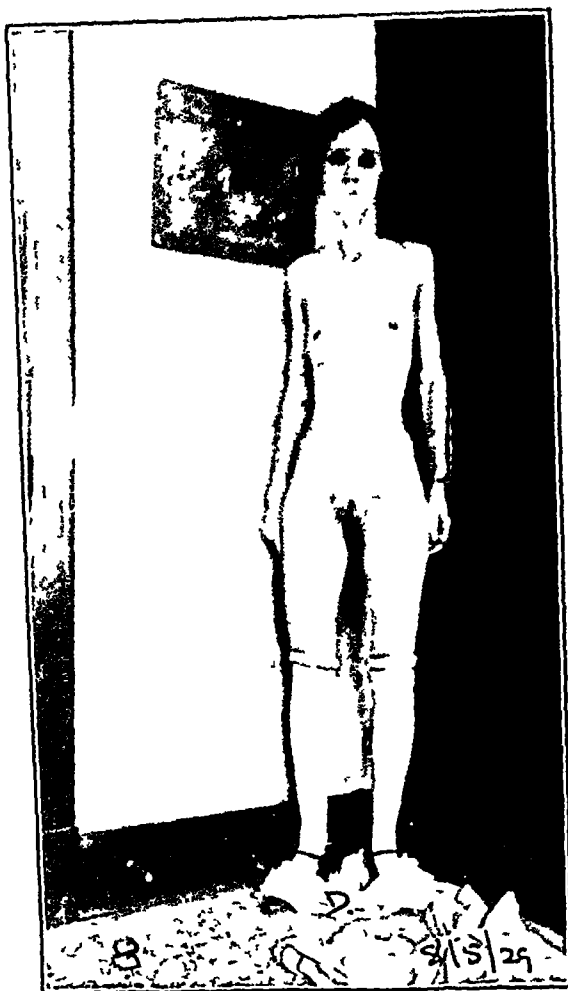


FIG 2—Case 2

**CASE 1** Mrs S Megalosplanchnic or broad type (note proportion between the transverse and longitudinal diameters) Massive pendulous abdomen that causes drag, with resultant backward inclination of spine and producing disturbance in function of the abdominal organs The chronic constipation cleared up when dietary, mechanical, and repeated exercises for the abdominal muscles were instituted

**CASE 2** Microsplanchnic or long type Miss D Age 35 Weight 96 Height 169 cm

**Chief complaint** Periodic attacks of epigastric heaviness, with nausea and vomiting after meals, of many years duration, not influenced by diet or alkali Previous diagnosis, ulcer stomach

**Physical examination** Dolichomorphic type, lordosis, gastropptosis, enteroptosis, metabolism, plus II

Fractional gastric showed no free, and but 12 total acid, at the end of one hour

On a program of forced diet with abdominal exercises, and support, she has gained 24½ pounds, and has been symptom free for a period of 4 months This case illustrates the importance of the study of constitutional make-up in evaluating symptoms

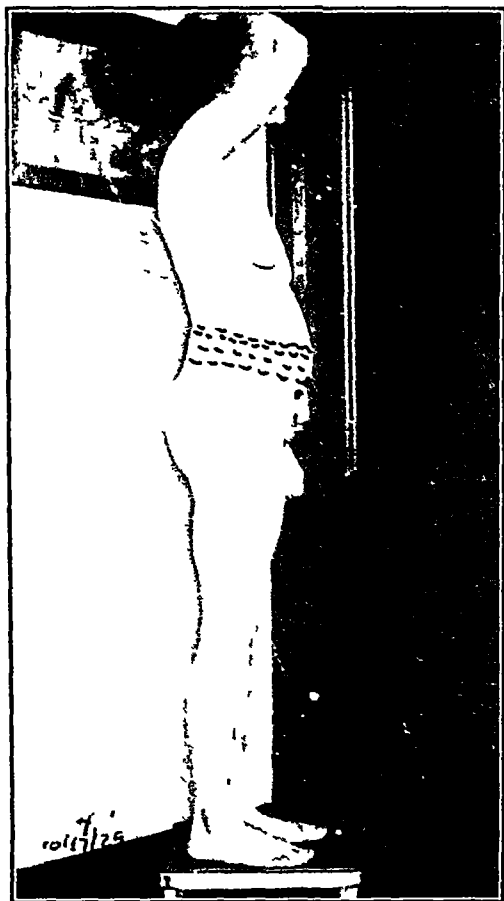


FIG 3—Case 3 B right

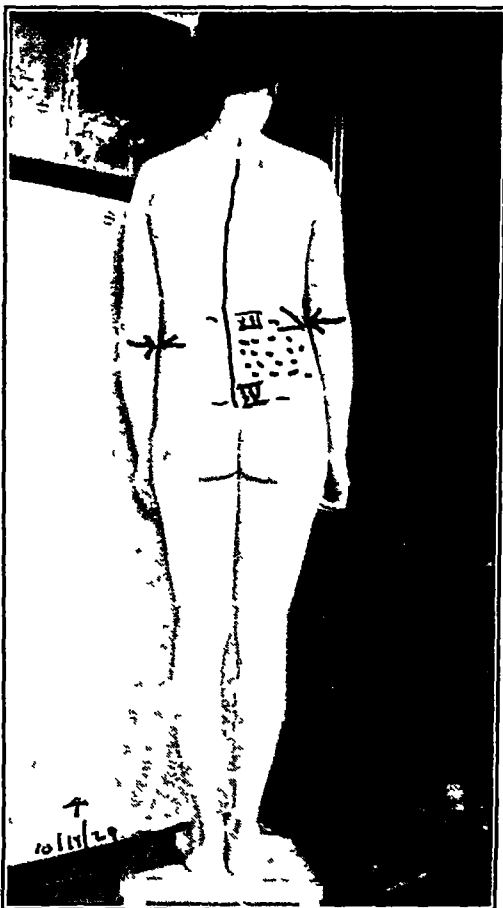


FIG 4—Case 3 A left

CASE 3 Mrs A Chief complaint Profund constipation, abdominal distention, nausea with occasional vomiting, melancholia, nervousness, irritability

Physical examination Dorsal and lumbar scoliosis, left pelvis one inch shorter than right, pendulous abdomen with mass in left lower abdomen, which disappeared under bowel therapy, marked anterior curve of lumbar spine, skin hyperesthesia, 10th dorsal to 3rd lumbar area, bilateral

Constipation and gastro-intestinal symptoms cleared up following mechanical correction of the anatomic disturbance together with dietary management and proper exercises for the spine and abdominal muscles

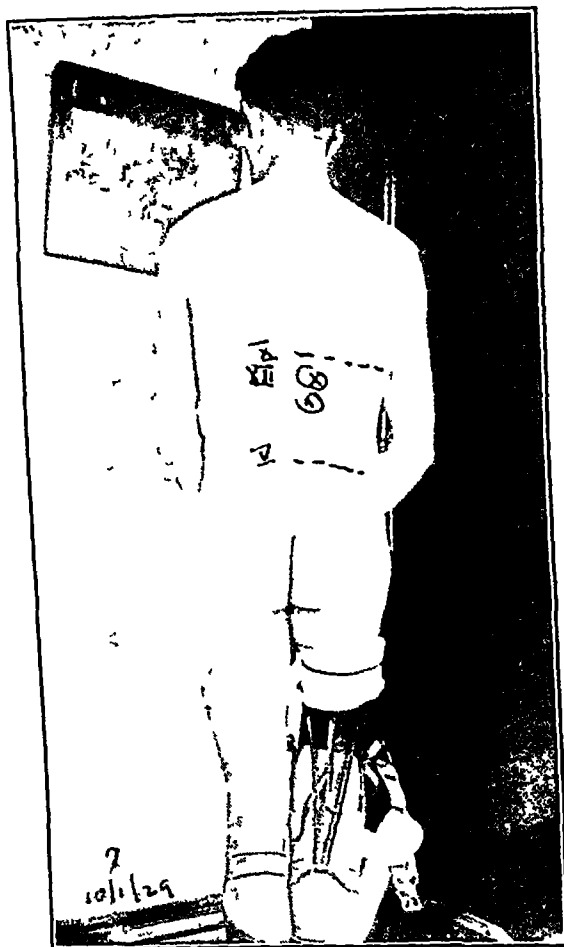


FIG 5—Case 4 A left

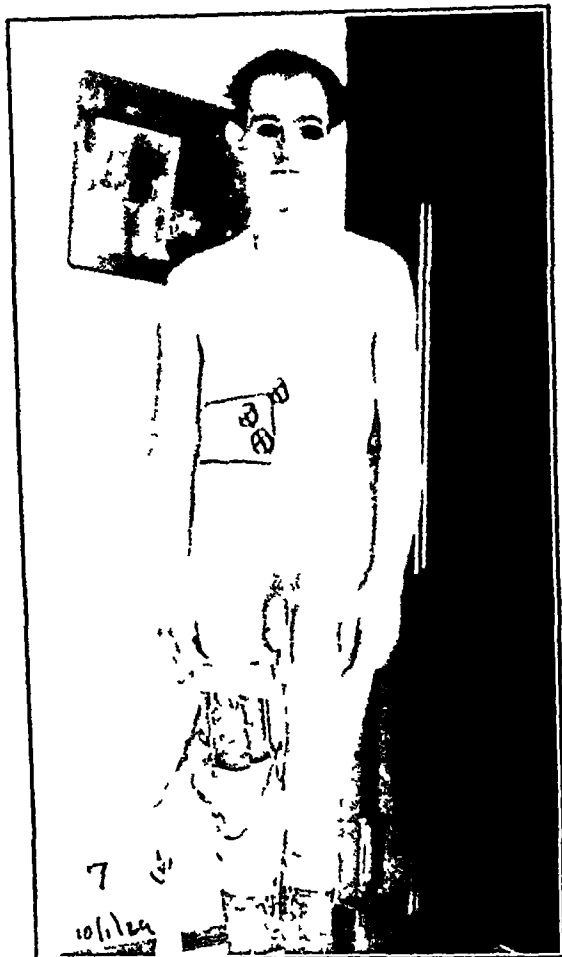


FIG 6—Case 4 B right

**CASE 4** Mr P O Chief complaint Indigestion, epigastric pains of years' duration periodic, seasonal, rhythmical, pain occurs two hours after meals, relieved by food or soda bicarbonate, but reappears one-half hour later, pain constant, localized, non-radiating in character

**Physical examination** Normal type with hypothyroidism and with amputation of right leg below knee, producing a mechanical disturbance in posture when walking Definite skin hyperesthesia 10th dorsal to 5th lumbar with pressure zone, same segments, right side

**X-Ray diagnosis**, ulcer duodeni, lesser curvature Fractional gastric analysis showed marked hyperacidity with occult blood present

Symptoms subsided upon correction of mechanical disturbance in addition to alkali therapy It is worthy of note that the above symptoms on former occasions did not respond to alkali therapy

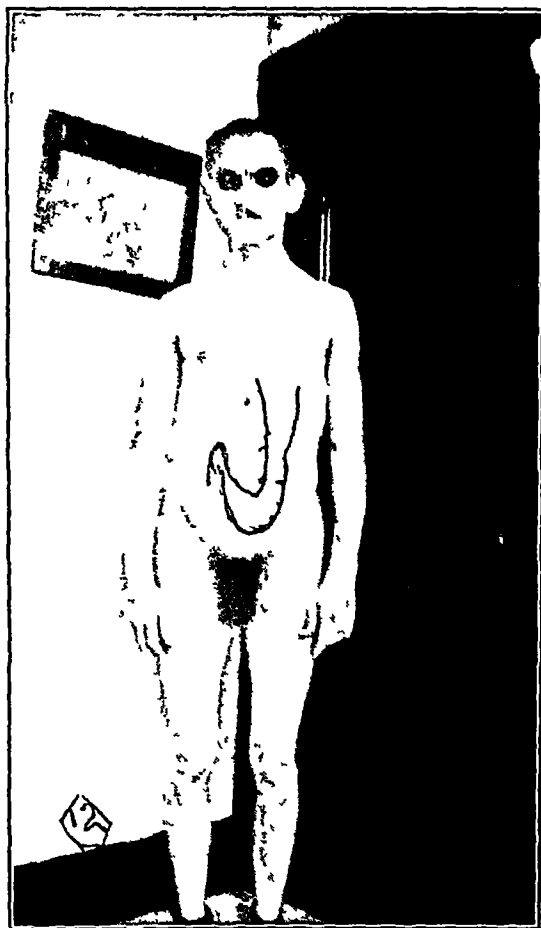


FIG 7—Case 5

CASE 5 P H Chief complaint Epigastric discomfort, nausea, pain and vomiting, after meals, periodical, rhythmical, definite

Physical Dolichomorphic type with hyperthyroidism, associated with hyperadrenalism, no focal infection found

X-Ray Ulcus duodeni and ulcus gastrica, lesser curvature

Fractional gastric, hypersecretion and hyperchlorhydria

Progress Temporary response to atropine and alkali-therapy and dietary management  
Definite response to non-specific protein therapy, calcium, and parathyroid and sedatives

Remarks This case clearly indicates the role of the thyroid and adrenal type of constitution in producing gastric manifestation. It is this type of ulcer case that does not respond to medical or surgical ulcer therapy, unless attention be directed to the endocrine glands



FIG 8—Case 6 A left

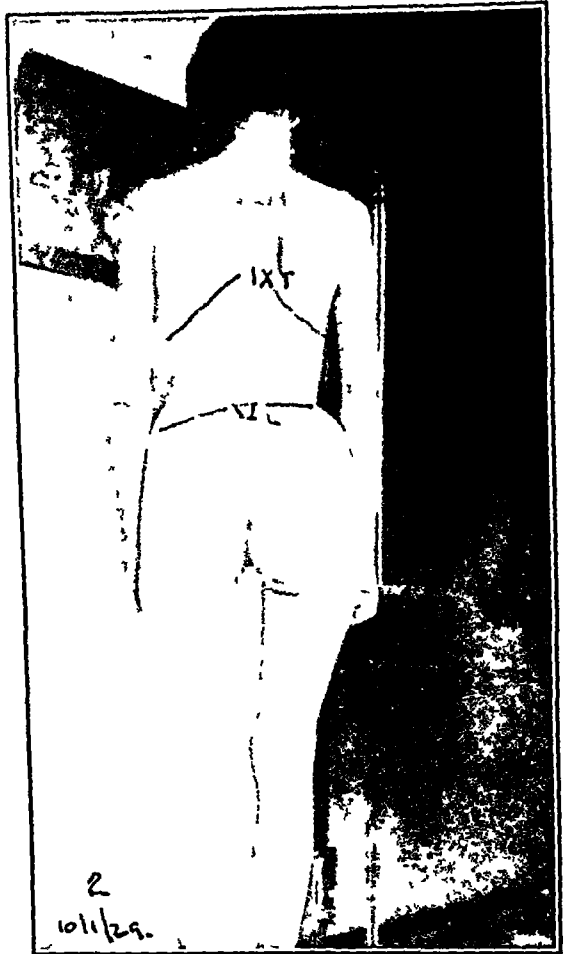


FIG 9—Case 6 B right

CASE 6 Mrs T Age 39 Chief complaint Loss of weight, weakness, nausea, vomiting, periodic, several years' duration, vomiting one-half to one hour after meals, has been constant for four months

Physical Microsplanchnic type, emaciated with definite skeletal deformity, producing definite change in size and shape of abdominal cavity An example of the influence of a skeletal deformity in producing gastric symptoms

Skin hyperesthesia from 9th thoracic to 4th lumbar segment

Laboratory tests negative, no evidence of lues

Progress, symptoms abated under exercise, diet and proper mechanical support Patient gained 20 pounds and is symptom free

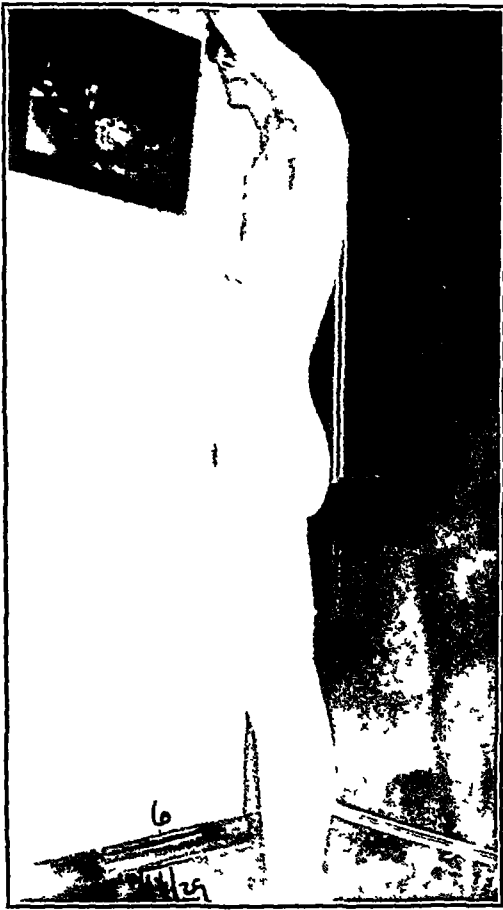


FIG 10—Case 7

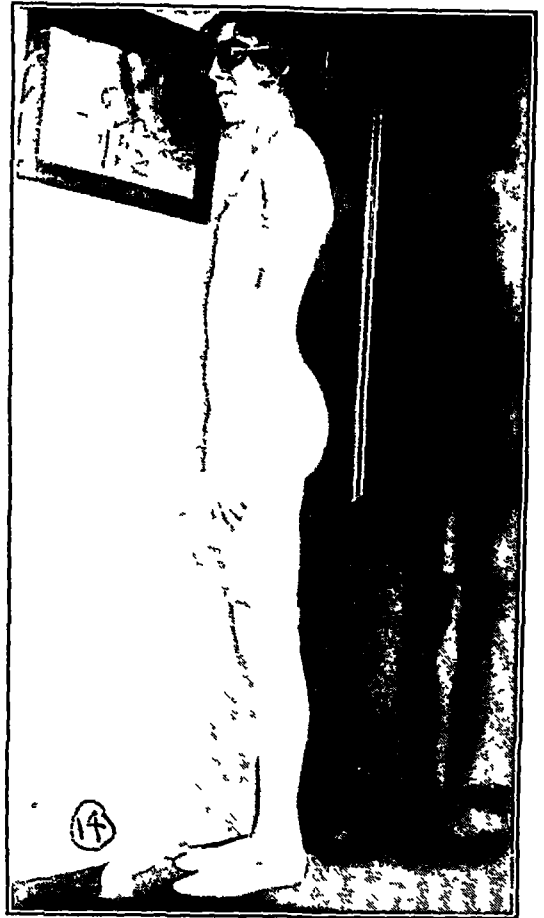


FIG 11—Case 8

CASE 7 Mrs H Dolichomorphic type with hyperpituitarism and hyperthyroidism  
Chief complaint Indigestion, loss in weight, severe constipation, gaseous distention

Physical examination Tall, emaciated, individual, flat chest, dorsal kyphosis with accentuated anterior lumbar curvature (note faulty posture)

R-Ray plate chest positive for active tuberculosis Stomach lies on floor of pelvis  
Fractional gastric analysis shows an achylia

Under a program of forced feeding, rest and abdominal support, patient gained weight and was free from symptoms Pulmonary tuberculosis causing gastric symptoms is not uncommon in this constitutional type Correction of the postural deformity by abdominal support, which increased intra-abdominal tension, often gives symptomatic relief

CASE 8 Miss R Age 19 Weight 91 pounds Infantile type of constitution associated with hyperthyroidism

Chief complaint Pain entire right side of abdomen, six months' duration

Physical examination Infantile type, small bones, flat chest, dorsal kyphosis with anterior curvature of lumbar area

Patient gained weight and was symptom free under a program of forced feeding, rest, Lugol's solution, quartz-light and abdominal support This type seems to respond when the intra-abdominal tension is increased by increased abdominal fat and by a mechanical support



FIG 12—Case 9

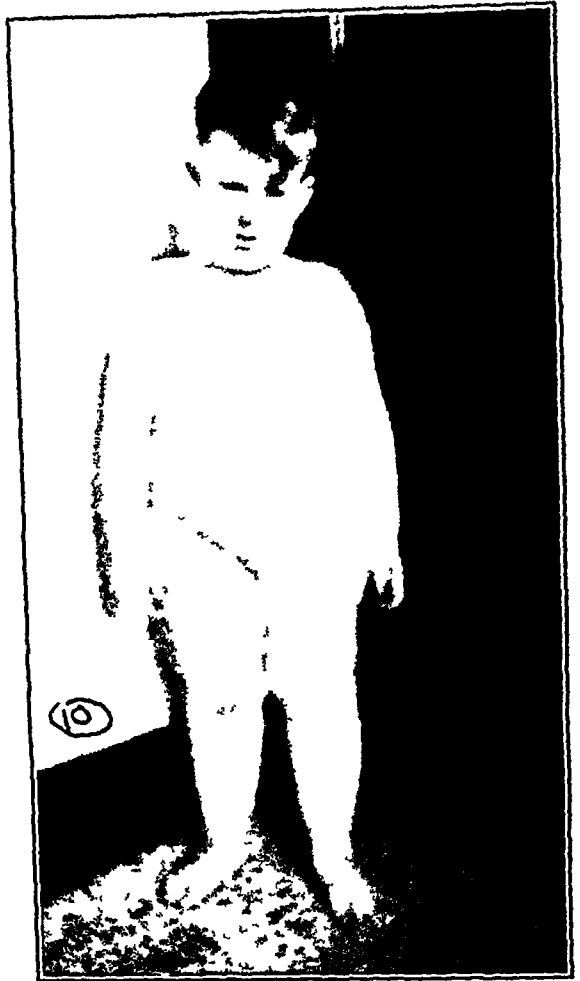


FIG 13—Case 10

CASE 9 Mrs F Chief complaint was burning in the epigastrium, with a hungry feeling, she was unable to satisfy

This case illustrates the mechanistic factor and its relationship to constitutional skeletal deformity, in this case a bilateral dislocation of both femurs The postural deformity probably caused pressure on the vascular supply or in the ganglia Abdominal support partially remedies her postural deformity, bringing about relief of her gastric disturbance *Wassermann* 4+ positive Specific measures instituted

CASE 10 A C Chief complaint Incontinence of urine and feces since birth, obesity, incorrigible

Physical examination Typical example of exudative diathesis in childhood Age 5, weight, 82 pounds, height, 45 inches (normal 43 pounds, 45 inches)

Past medical history Unable to sit upright until two years of age, and only then, after intensive x-ray therapy over thymus

Obese, undescended testes, small penis Patient very difficult to manage, very sensitive to external stimuli

Progress Incontinence of urine and feces cleared up under pituitrin and thyroid medication

This case illustrates the role played by the endocrines in constitutional inadequacy



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# Agranulocytosis

By WILLIAM HENRY GORDON, M D, *Detroit, Michigan*

**A**GRANULOCYTOSIS, Agranulocytic Angina or Malignant Neutropenia was first described in full in the German literature by W Schultz in 1922. Since this report a total of about eighty papers have been written describing this condition. The first appearance in American literature was in the paper of W A Moore and H S Wieder in the Journal of the American Medical Association, August 1925.

Schilling says "the term 'agranulocytosis' has come into the nomenclature on account of its brevity. It is incorrect the name of 'Agranulocytes' was originally chosen for 'neutrophils without granulations' of leukaemias. By 'Agranulocytosis' is meant an increase in these atypical neutrophils, which is not intended." He therefore calls the disease "Malignant Neutropenia."

This condition may be a definite disease entity, or the result of (a) a chemical poisoning or (b) some chronic disease, diseases or infections. It can be defined as a very severe ulcerative angina, usually manifested by signs of an acute infection and associated with marked prostration, extreme leukopenia with lack of granulocytes.

The etiology at present is unknown. Some observers believe it to be a chronic Vincent's Angina. Others believe it to be a very severe sepsis in

which Vincent's spirillum is only a laboratory finding, still others believe it to be the complication of a long protracted illness such as hypertension and chronic gall bladder disease. A few believe it to be the result of poisoning by chemicals after treatment with some drug of the benzene ring series. Many think it to be a new disease. It occurs in both males and females. The youngest case on record, that of N Christof's, was 2 weeks old and the oldest, herein reported, was 66 years of age. About 90 per cent of the reported cases have been females. David believes the blood picture due to a defect of the cell distribution and not to faulty formation. Skiles believes "it may be a specific infection in the gangrenous areas which secretes a specific toxin against the granulocytes," or "it may be a primary infection of the bone marrow resulting in a drop in the formation of granulocytes with a lowering of resistance of the patient. This might make the patient subject to any intercurrent infection, with resulting necrosis and death."

Another observer thinks that there is some injury to the reticuloendothelial cells of the liver. Hirsch stresses the point that "it is certain that it is not of tonsillar origin, for many times the tonsils become infected some time after the beginning stage and occasionally do not become involved at all."

Case No 3 had had tonsils well removed Schultz "It may be assumed that the affection involves an extensive injury of the spinal cord in the domain of the granulocytic system, caused by infection"

Several authors have attributed the disease to bacterial origin Lovett reproduced the disease in guinea pig with bacillus pyocyaneus Many of the reported cases had positive blood culture to streptococcus and staphylococcus Hill's case occurred in a woman of 35 years of age and started after extraction of a tooth the smear of which showed Vincent's and other organisms Several cases have been reported after the removal of very severely infected teeth with positive smears to streptococcus and Vincent's (Vos)

Edith Peritz's case and cases No 2 and No 3 of this paper were being studied in the hospital for gall bladder disease when they suddenly developed all the signs of an acute head cold and this was very quickly followed by the typical picture of the disease

Many cases have been sent to the hospital for diphtheria and upon a study they have had negative cultures with all the signs of this disease and the diagnosis has been made by white blood count and also at autopsy (Zikowsky)

*Pathology* The mucous membranes throughout (tongue, throat, tonsils, larynx, pharynx, vagina, rectum and whole intestinal tract) have huge ulcerative areas (These differ from ordinary ulcerative diseases in that microscopic section shows the usual inflammatory reaction at the border of the lesion to be absent) The liver, spleen and lymph glands may be

slightly enlarged or unchanged Section of them shows nothing of importance The bone marrow is liquid and is anything from a straw color to an intense red It contains few cells There is marked absence of granular cells and a definite granulocytic aplasia of the bone marrow It contains many plasma cells and lymphocytes (Schilling) One case reported by George J Kastlin showed endothelial hyperplasia in spleen, lymph nodes and bone marrow Some cases showed skin lesions, others showed petechial hemorrhages late In the study of the bone marrow the work of Zadek, Schultz and Jacobwitz is very important They removed bone marrow from the sternum during the height of the disease These specimens were cell poor and were very similar to the marrow at autopsy, that is they contained no granulocytic elements This work was repeated by Robert W Buck in his case of "Agranulocytosis with Anal Ulcer" reported in the J A M A, November 9, 1929 He removed section specimens of bone marrow in his study of the case before it came to autopsy

There is an increase in the reticulo-endothelial cells of the bone marrow, spleen and circulating blood These cells contained small oxydase granules which have been attributed by Hirschfeld to degenerative changes

*Symptoms* The patient may be perfectly well or under the care of his physician for some chronic disease K Tokue and M Yasumato were treating a child 4 years old for fracture of the skull when he developed the disease Hunter's case was under treatment for fracture of the tibia Ehrmann and Preuss were investigating

the etiology of jaundice in their case Leon Bromberg and Paul Murphy had given prophylactic typhoid vaccine and Bantz's patient had tuberculous arthritis when he developed the disease. Suddenly while at home or in the hospital a patient may develop all the acute symptoms of cold, i.e. high fever, chills, severe sore throat and coryza, and within 24 to 48 hours usually but even after several days the patient has dysphagia, ulcerative then gangrenous stomatitis, swelling of the neck at the angle of the jaw, malaise, marked toxicity and prostration. Icterus occurs in over 50 per cent of the cases. Lauter observed that "the height of the disease occurred on the day gangrene appeared in the mouth." Liver, spleen, and lymph glands may be normal in size. Often the lymph glands are enlarged. The toxic symptoms become much worse and are followed by delirium and death.

*Laboratory Data* If a blood count is taken early in the disease it may be normal in every manner. The platelet count is normal. The coagulation and bleeding time has been normal except in one case reported by Kastlin. The hemoglobin, and red blood cells have been normal in the majority of the cases. Zadek reported two cases with 29 and 49 per cent hemoglobin, respectively. The white blood count has been the interesting and diagnostic factor. It has been low in all cases and gradually decreased to nothing if the disease proved fatal. The granulocytes became less and less and the lymphocytes relatively increased.

In the few cases which have recovered the white count returned gradually to normal. These cases upon

careful cytologic study of the leukocytes showed early in their course an increase in the large monocytes over 14 to 20 per cent. They also showed a Schilling index which had an early increase in the myelocytes and young cells. These latter laboratory procedures have been of value in determining the prognosis.

The course of the disease is usually acute and very rapid. A few cases have lived weeks and months. The prostration and ulceration shows marked progress from morning to night. The white blood count and differential shows definite change from hour to hour. It absolutely disappears in the majority of cases before death. A few cases recover or have remissions.

The prognosis is usually fatal after a very acute onset and course. The lesions spread rapidly. Those few cases which have recovered show the high per cent of monocytes and the Schilling shift early as mentioned in the laboratory study.

*Differential Diagnosis* The disease must be differentiated from Pernicious Anemia (Biermer's Anemia), Severe Secondary Anemia, Aleukemic Leukemia, Monocytosis, Sepsis, Kala Azar, Noma, Diphtheria and Black Diphtheria, Vincent's Angina, Aplastic Anemia and Thrombocytopenic Purpura. It is diagnosed from

(1) Pernicious Anemia by the extreme prostration, angina and the absence of the typical blood picture of a low red blood count, high color index and usually normal white blood count.

(2) Severe Secondary Anemia by the history, and the absence of the blood picture of a uniform definite de-

crease in both red and white blood cells with a normal differential

(3) Aleukemic Leukemia by the blood picture and symptoms and absence of generalized increasing enlargement of the lymph glands

(4) Monocytosis by the decreased instead of increased white blood cell count with predominance of monocytic cells

(5) Sepsis by history, physical findings and blood picture

(6) Kala-Azar as the latter is common only in Asia and Soudan and by the lack of large spleen, length of irregular fever, progressive anemia and cachexia, and in Kala-Azar spleen puncture shows Leishman-Donovan bodies

(7) Noma by ulceration of mucous membranes of mouth without change in blood picture

(8) Diphtheria and Black Diphtheria by absence of Klebs-Loeffler bacillus

(9) Vincent's Angina by absence of fusiform bacillus and spirillum in sufficient numbers

(10) Aplastic Anemia by history of some cause as Salvarsan treatment, etc

(11) Thrombocytopenic Purpura by absence of a large spleen, low platelet count and not typical picture

The disease may occur in conjunction with some of the above, as William Allen reported a case of Agranulocytic Angina with Thrombocytopenic Purpura

The diagnosis is made by history, onset and course of the disease and finally by the white blood count with lack of granulocytes

In the treatment of the disease many drugs and types of therapy have been tried. The following Omnadin, Neo-salvarsan, Iion, Arsenic, Liver, bone marrow, various nuclein extracts (such as nucleic acid and leukocytic extract), streptococcus serum, intravenous medication with foreign proteins (especially typhoid), x-ray to spleen and long bones, ordinary blood transfusion and blood transfusion from a cured case have been suggested. One case reported by Finnegan was helped by transfusion. Otto Hoche used blood transfusion in three cases one of which recovered. Hart has had no results with the treatment and believes the disease to be hopeless. Freedman reports four cases as cured by x-ray therapy. No cases have been helped by arsenic or mercuriochrome. One case was helped by typhoid vaccine intravenously. Two cases (including case No 3, this paper) were helped and possibly cured (too early to give absolute report) by daily injections of nucleic acid.

The four cases which I wish to present are

#### CASE No 1—E B

Age 36 Female Unmarried Stenographer Born in Saginaw Has been under my care since January 23, 1925, for Lues. During this time she has had several courses of neo-salvarsan, bismuth and mercury, the last course having ended in December, 1926. Patient gives a negative family history. Past history negative with the exception of lues (Patient has a loose moral character). Menstrual history negative.

*Present Illness*—On September 18, 1928, she came to the office because of right sided sore throat and pain in the ear (drum membrane was congested), and was diagnosed right tonsillitis (early quinsy) and right otitis media. On September 21, 1929 I saw

1012

William Henry Gordon

CASE NO. 1

V-9 1046 9-17-28

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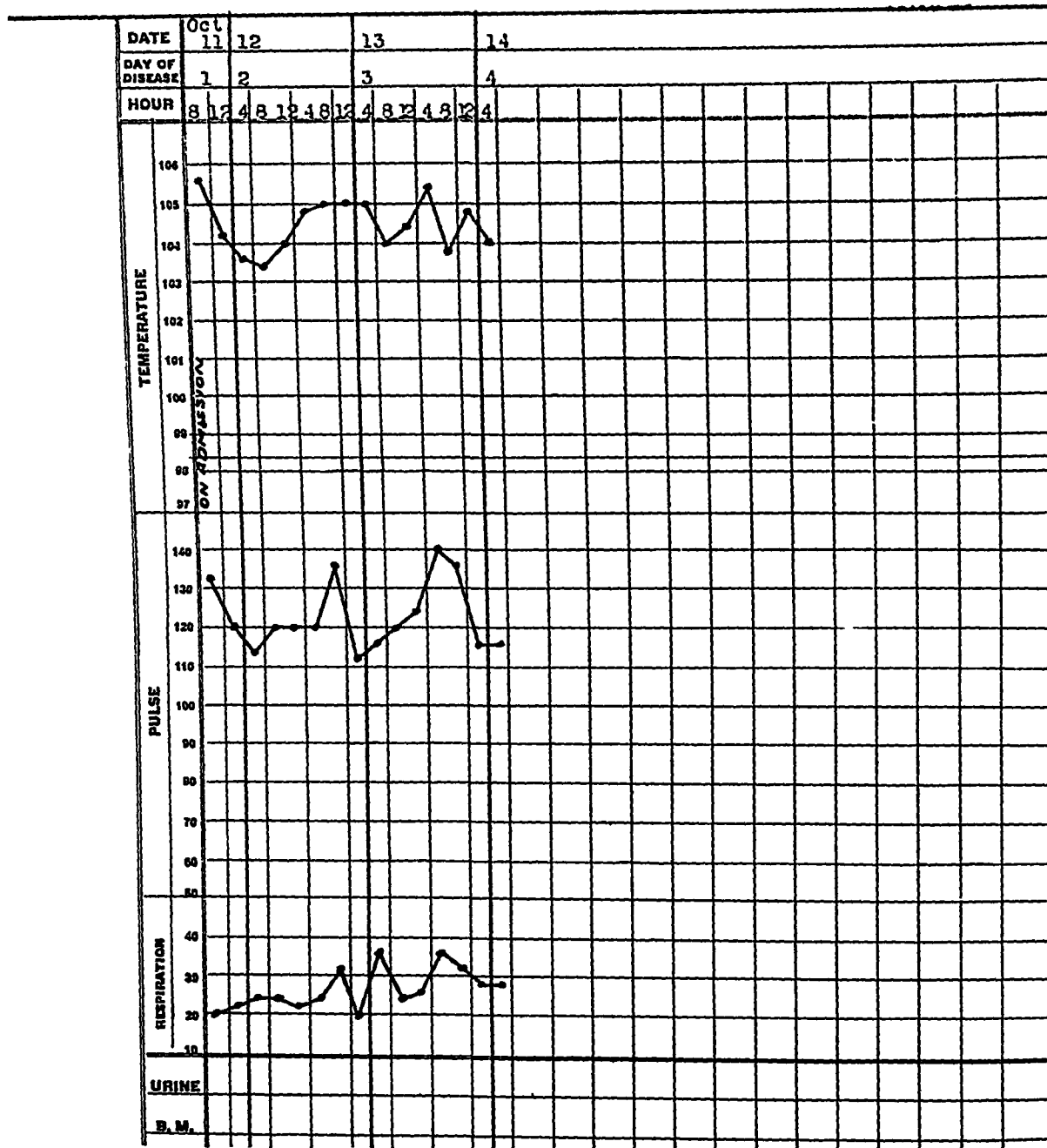


CHART I

her at her home and she had a membrane over both tonsils and was given 10,000 units of diphtheria antitoxin (Culture taken at that time was returned negative) September 22, she was given 20,000 units more and a second culture was reported negative September 23, the left tonsils appeared healed but the right tonsil ulcer was not healed and appeared to be punched out and contained a gray slough. A question of tertiary lues was brought up and she was given 50 mg of bismuth hydroxide intravenously. The ulcer began to heal and did heal by September 30, 1928.

On October 9, 1928, patient came to the office because of painful and swollen glands in the neck at the angle of the jaw. Her temperature was 105. WBC was 800, all lymphocytes. A direct smear showed staph and strept and her soft palate and tonsils showed severe ulceration with a grayish membrane. She was sent to the hospital and entered October 11, 1928, with a chief complaint of severe sore throat, difficulty in swallowing and respiratory embarrassment. On entrance to the hospital the following note was made: Patient had swelling of the neck and jaw especially at angle of jaws with a flushed facies and her skin showed a peculiar yellowish icteric tinge. She appeared very ill but was rational and was very reticent and non-co-operative. Her right tonsil area was replaced by ulceration and covered by a gray-green exudate and was surrounded by considerable edema of the fauces, pharynx and epiglottis. Left side was covered by the same exudate, was reddened and edematous. The inflamed areas were acutely tender and there was swelling of the right submaxillary region which extended over the entire lower jaw and especially at the angles and progressed up to the time of demise. The swollen area was not fluctuant. The vagina showed ulcers.

#### *The Laboratory Data*

May, 1928 WBC 7500, Hgb 90%, RBC 4,800,000 Normal Diff Wasserman 4 plus Kahn 4 plus

Oct, 11, 1928 WBC 800, all lymph Oct 12, 1928 WBC 300, all lymph RBC 3, 140,000, Hgb 50% Oct 14, 1928 WBC 300, all lymph Urine neg at all examina-

tions Temperature ranged from 103 to 140 Resp 28 to 40 Blood pressure 100/70 moist râles were heard at both bases of lungs Otherwise findings were negative Patient died at 1 45 P M, Oct 14, 1928

#### CASE No 2—Mrs H H

Age 66 Female Married Housewife Born in Elk Rapids, Mich Has been under care for 3½ years for hypertension, chronic cholecystitis and myocarditis *Family history* negative except 2 sisters died of cancer *Menstrual history*—Menopause at 50 by hysterectomy Patient married at 27 years, never pregnant Husband living and well *Past history*—Has always been ill Operated in 1910 for hysterectomy, appendectomy and hemorrhoidectomy Has been deaf for 28 years In October, 1926, was jaundiced with swelling of the legs and tender gall bladder In November, 1926, had a left otitis media and influenza

Her positive examination before present illness showed blood pressure 160 to 224 over 70 to 110 Pulse 96 Nerve deafness both ears Pale conjunctivae Arcus senilis Septic tonsils Upper and lower plates excepting the upper front Neck negative Heart enlarged, distant sounds, presystolic murmur at apex not transmitted Abdomen midline scar from umbilicus to pubis Liver enlarged 2 f b below c m and tenderness in RUQ Reflexes normal Rectum negative Gynecological No uterus, no cervix

Urine showed albumin on several examinations Blood chemistry normal Wasserman negative RBC 4,300,000, WBC 7500, Hgb 75%, Differential normal GI examination showed chronic cholecystitis Our diagnosis was chronic cholecystitis, myocarditis and hypertension During all my observations this patient always complained of stomach trouble and frequent colds

In February, 1929, patient had a lower right third molar removed and following this had a severe attack of gall bladder pain accompanied by dizziness Pain in RUQ She also had high blood pressure with distress in the abdomen and chest This was accompanied by frequent sore throats As patient lived in Pontiac and the attacks were becoming more frequent I advised her





to enter the hospital here which she did June 3, 1929

On entrance to the hospital she had RBC 4,280,000, WBC 3200, Differential 100 lymph CI 93 On June 4, patient developed a severe sore throat, with coryza and marked prostration The nasopharynx and palate were a dry dull red color With this she showed a progressive decrease in the WBC with a relative increase in the lymphocytes, and absence of granulocytes Also progressive ulceration of the throat, tonsils, nasopharynx and larynx and uvula She also had difficulty in swallowing and talking Her temperature went to 104, pulse 40 and respirations 40

#### Laboratory Data (June, 1929)

June 4, Hgb 70%, RBC 4,280,000, WBC 3,200, all lymph CI 83

June 5, 10 45 P M WBC 1300, 25 cells counted, all lymph

June 6, A M Hgb 70% RBC 3,490,000 WBC 1350, 20 cells, all lymph

June 6, 5 30 P M WBC 700, 30 cells found, all lymph

June 7, 9 A M WBC 800, 10 cells found, all lymph

June 7, 9 30 A M 25,000,000 typhoid bacilli injected intravenously

June 7, 10 30 A M WBC 700, cells all lymph

June 7, 11 30 A M Post typhoid chill

June 7, 12 15 P M WBC 650, all lymph

June 7, 7 30 P M WBC 600, all lymph

June 7, 9 45 P M Given 315 cc citrate blood

June 8, 9 A M WBC 500 cells, all lymph Given 5 cc leukocytic extract

June 8, 11 A M WBC 650 cells, all lymph

June 8, 7 P M WBC 500 cells, all lymph

June 9, 9 20 A M Died

Urine showed 2 plus albumin, otherwise negative Stools neg NCN 30 BS 125 Wasserman negative

Postmortem examination was made of Case No 2 with the following positive findings Generalized ulceration of the tonsils, soft palate, nasopharynx and larynx Areas

of ulceration in the stomach, ileum, jejunum and colon, also rectum Also ulcers in the vagina Marked swelling of the neck at the angle of the jaw down Atrophy of the bone marrow which was a pale straw color and contained no cells upon microscopic study Chronic myocarditis, cholecystitis, hepatitis, and nephritis

#### CASE No 3—Mrs O W

Age 33 Female, Born in Indiana Lived in Detroit for past 5 years Family history negative Menstrual history negative Married 9 years, 2 children, ages 6 and 2 years, living and well Husband living and well No miscarriages Past history—Usual childhood diseases Hysterectomy, appendectomy, perineorrhaphy Has had cholecystitis for 6 years, also chronic accessory sinus diseases Patient was admitted to Harper Hospital for study of her gall bladder and sinuses She was to have the sinuses treated and probably a submucous operation, when she developed a severe cold with a sore throat and was sent home to recuperate on November 18, 1929, without any operative therapeutics Her physical examination while in the hospital was negative except for the following Blood pressure 108/70 Tenderness over all accessory sinuses Slight tenderness and muscle spasm in right upper quadrant and epigastric region, and pharyngitis Her laboratory data was 11-12-24 Hgb 70%, RBC 4,400,000, WBC 8400, P 74, L 20, M 4, E 2, RBC normal 11-11-29 Urine negative 11-12-29 PSP test 1st 15 min, 60%, 2d 30 min 20%, 3d 60 min 10%, total 90% 11-12-29 Duodenal drainage 275 cc clear greenish amber fluid, no wbc or bacteria seen NCN 40 mgs Sugar 0.090% Icteric Index 10 Van den Bergh's Direct and Indirect slightly positive X-Ray dorsal and lumbosacral spine shows a lumbarization of the first sacral segment and evidence of irritative changes about the left sacroiliac synchondrosis 8-27-29 X-ray of the chest and gastrointestinal series shows no front parenchymal involvement of either lung, cardiac and aortic shadows are of normal size No organic lesion of stomach, duodenum, small or large bowel Definite pericecal tender-



FIG 1. Case 2, Larynx



ness, cecum being low in pelvis. Non-filling of gall bladder with the dye.

On 11-24-29, one week after her discharge from the hospital, I was called to see her at the house, and found her with complaint of sore throat and severe prostration. Examination showed temperature 103, markedly prostrated patient, with icteric tinge to the skin. There was definite anemia present with no ulceration. I sent her immediately to the hospital with the provisional diagnosis of agranulocytic anemia. Blood count on admission to the hospital, November 24, 1929, showed 85 per cent hemoglobin, 4,600,000 red cells, 2000 white cells and differential count, Polymorphonuclears only 4 per cent, lymphocytes 88 per cent, large monocytes 8 per cent, red blood cells were normal. I gave her immediately 1 cc of nucleic acid. Her blood counts while in the hospital were as follow at the end of this report. Her temperature rose to 103 on the second day after admittance, but dropped to normal on the fourth day and remained normal. Her temperature was 99 on admittance and pulse was 120, but pulse returned to 80 on the fourth day in the hospital. Smears of nose and throat were negative. Patient continued to improve and on the tenth day was discharged from the hospital apparently recovered.

Treatment given was nucleic acid, 1 ampoule daily, leukocytic extract was given after blood transfusion of 450 cc which was given by the indirect method. After the transfusion, patient continued to improve. Her final blood count on December 13, 1929 was WBC 8800, Differential Small 25%, Trans, 2% and Polys 73%.

*Blood Counts While in the Hospital—*  
(11-25-29 to 12-9-29)

11-25-29, Hgb 85%, RBC 4,600,000, WBC 2000, P 4, L 88, M 8, RBC normal

11-26-29, 11 A M WBC 1100, P 8, L 82, M 10, RBC normal

11-26-29, 1 P M WBC 2300, P 4, L 86, M 10, RBC normal

11-26-29 4 P M WBC 3050, P 6, L 90, M 4, RBC normal. Blood transfusion, 450 cc

11-26-29, 10 P M WBC 2850, P 4, L 92, M 6, RBC normal

11-27-29, 8 A M WBC 1874, P 37, L 63, RBC normal

11-27-29 Schilling index, M=7, Y=8, R=18, P=1

11-27-29, 1 P M WBC 1950, P 15, L 55, M O RBC normal

11-27-29, 8 P M WBC 2225, P 49, L 51, 2 Turck cells seen

11-28-29, 8 A M WBC 2210, P 18, L 51, M 1

11-28-29, 1 P M WBC 3000, P 40, L 55, M 5, some of the polys being to take on cosmophilic character

11-28-29, 8 P M WBC 3075, P 11, L 48, M 8

11-29-29, 8 A M WBC 3185, P 18, L 48, M 4, some polys appear natural

11-29-29, 8 P M WBC 4575, P 45, L 53, M 2

11-30-29, 8 A M WBC 4625, P 56, L 42, M 2

11-30-29, 8 P M WBC 5630, P 66, L 30, M 4

12-1-29, M A M WBC, 10, 225, P 81, L 19, RBC normal

12-1-29, 8 P M WBC 10,050, P 82, L 18, normal morph

12-2-29, WBC 7,750, P 65, L 35, normal morph

12-3-29, WBC 7,500, P 60, 4, 39, M 1, normal morph

12-4-29, WBC 8,150, P 72, L 28, normal morph

12-5-29, WBC 7,550, P 68, L 32, normal morph

12-6-29, WBC 7,950, P 62, L 38, normal morph

12-9-29, WBC 6,650, P 74, L 25, M 1

11-26-29, NCN 30 mgs, sugar 0.083% CO<sub>2</sub> combining power 55 i, vol % Icteric Index 4. Van den Bergh Direct neg, Indirect—slightly positive. 11-29-29 Blood Wasserman neg

CASE No 4—W R

Age 55 Male Married Business advertising. Family history negative except mother died of Tbc at 48. Past history—Typhoid and pneumonia at five years. Remittent fever at 18 years, duration 9 weeks

Pneumonia at 42, mild case Denies venereal

*Present Illness*—Came to the hospital May 16, 1928 for study of cause of dizziness, shortness of breath and feeling of pressure over chest. He had recently noted that upon walking any distance he became dizzy and had to stop because of choking feeling. After resting a few minutes he could proceed. This had been going on for three months. For a time up to three weeks ago he improved by lessening his activities but it has returned and become more severe. Six weeks ago while walking he became very dizzy, faint, and experienced blurred vision with pressure in chest. He has been in bed for the past two weeks.

Physical examination was negative with these positive exceptions: well developed, pale, male. Tonsils enlarged and septic. Nasopharynx congested. Heart enlarged, pulse 60, irregular, slow, irregular sounds. At mitral and tricuspid areas 1st sound is low pitch, booming in character, 2nd sound cannot be heard. At pulmonic area, 1st sound present, 2nd absent. At aortic area 1st and 2nd sounds barely audible and not distinct. Lungs were neg. Abdomen and extremities neg. Electrocardiogram showed sino-auricular block with occasional nodal rhythm. 5-17-28 RBC 4840,000, Hgb 90%, CI 9, WBC 7400, P 74, L 24, M 2, Morph normal. Urine neg except few casts. Blood sugar 0.105. NCN 30 mgs. Blood Wasserman neg. BMC 13%. Patient was discharged on May 20, 1928 with diagnosis of Partial heart block and chronic tonsillitis.

Patient returned to the hospital May 26, 1928, because on May 21st he developed headache and sore throat with pains and aches throughout body. These symptoms increased and on May 23, the physician found slight congestion of the throat and that patient was very toxic. His temperature had ranged from 101 to 102 during the preceding 24 hours and was accompanied by a series of chills.

On May 24th the pains, sore throat and toxicity increased. Temperature was 104 and was accompanied by chills. Patient entered the hospital on May 26th with tem-

perature of 104.2, pulse 88 and respirations 24. Throat was very congested and inflamed and showed numerous grayish plaques in soft palate and pharynx. RBC 3,232,000, Hgb 70%, WBC 2200, P 0, L 89, 11, Blood pressure 65/40.

May 27th, 1928, WBC 1800, P 0, L 62, M 38. RBC normal in size and shape. He also had thrombotic hemorrhoids. Patient died May 28, 1928, 3:52 A.M. with diagnosis of agranulocytic angina. Autopsy showed the typical bone marrow findings. It also showed arterosclerosis of the coronary vessels and also the infarct in the bundle of His.

*Conclusions* Summing up the story of this condition in the literature and from clinical observation, I believe that we may conclude the following: (1) At the present time it is impossible to decide whether this is a definite disease entity or whether it is the complication of some group of medical conditions or the result of some drug or chemical poisoning. (2) The cardinal symptoms of the disease are its acute onset with all the signs of a severe cold such as coryza, sore throat, high fever, joint and body pains. This is followed by severe angina with ulcerations and a definite leukopenia with absence of the granulocytes. And, finally, extreme prostration and death in the large majority of cases. (3) The course and prognosis is usually short, severe and fatal with very few exceptions. Those few who recover, recover temporarily. (4) The pathology shows an absolute lack of inflammatory process in the tissue surrounding the lesions and the bone marrow shows a lack of granulocytic structures. (5) Study of the cytology of the leucocytes early helps in making an early and correct prognosis. (6) The treatment which has been varied

has been of no avail with these excep- by x-ray of the long bones and spleen  
tions a few cases have been im- and two cases were probably cured by  
proved by blood transfusions, a few the use of nuclemic acid injections

CASE NO. 4

P-1 111 1-12-8

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NAME \_\_\_\_\_ ADMISSION NO \_\_\_\_\_ DEPT NO \_\_\_\_\_

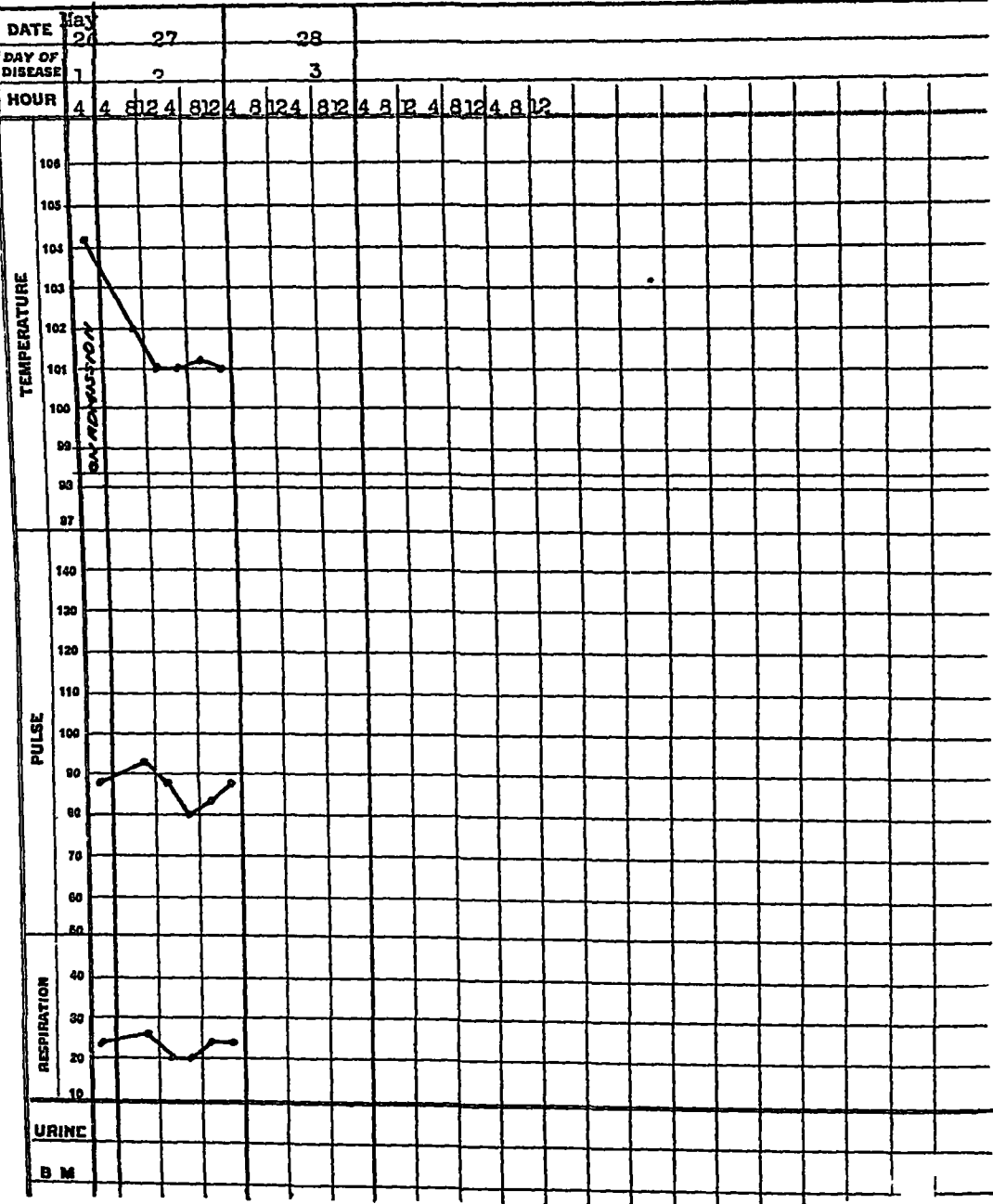


CHART 4

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# Massive Collapse (Atelectasis) of the Lung, With a Case Report

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**H**ISTORY While W. Pasteur<sup>(1, 2, 3)</sup> has been given credit for first describing massive pulmonary collapse as it is now understood, a review of the literature reveals the fact that the study of this condition in the first half of the nineteenth century gave rise to much discussion, usually under the term "carnification" of the lung. There seemed to be considerable confusion with reference to the relation of this condition to pneumonia and fetal atelectasis. Not until 1844 did Legendre and Bailey<sup>4</sup> establish by postmortem studies the identity of congenital atelectasis and acquired massive collapse. No doubt stimulated by the work of Legendre and Bailey, Mendelssohn<sup>5</sup> in 1845 and Traube<sup>6</sup> in 1846 experimentally produced massive collapse by occlusion of the bronchi. In 1879, Lichtheim<sup>7</sup> confirmed the above experiments and proved that collapse in that portion of the lung normally aerated by the occluded bronchus was a result of absorption of the air by the blood stream. By the simultaneous occlusion of a bronchus and ligation of the corresponding bronchial vessels, he established the fact that collapse would not occur when the circulation was inhibited. In 1910, Pasteur's third paper<sup>3</sup>

appeared under the title "Active Lobar Collapse of the Lung After Abdominal Operations." It was in this paper that cardiac displacement toward the affected side was clearly set forth as a significant diagnostic sign, and the definite relationship of massive collapse to surgery was first suggested. In two succeeding papers, 1911 and 1914, Pasteur<sup>8, 9</sup> brought the knowledge of this condition to such a state of perfection from a diagnostic standpoint that there was little room left for additions. In America, the writings of West<sup>10</sup>, Meigs<sup>11</sup> and Foster<sup>12</sup> are worthy of note. While these authors may have displayed a certain amount of originality, it seems that they made no important contributions to the knowledge existing at that time.

The rapidly increasing literature on this subject, with numerous case reports, serves to emphasize the frequent occurrence of the condition and its clinical significance. Bowen<sup>13</sup> points out the fact that during the six year period from 1921 to 1926 he was able to tabulate forty-eight papers dealing with massive collapse while in the one year 1927 he found half that number. Several of the papers appearing in the last few decades have dealt with the experimental production of massive

collapse but in the main they have only refined the experiments of Lichtheim and confirmed his results. Most noteworthy among these are the papers of Elliott and Dingley<sup>14</sup>, and more recently, Coiylos and Birnbaum<sup>15</sup>. The experiments carried on by the latter authors were controlled by repeated x-ray examinations and are quite convincing in their verification of the cause, the symptoms and the physical signs. The cumulative evidence, both clinical and experimental, is overwhelmingly in favor of bronchial obstruction of some type as the cause, and of mucous plugs in the bronchi as the most constant single factor.

In 1927 Doctor Gordon Wilson,<sup>16</sup> before the American Climatological and Clinical Association, reported the observation of a marked negative intrapleural pressure in this condition, first studied in a post-traumatic case in 1921. At the annual meeting of this association, May, 1928, Doctor Charles C. Habliston<sup>17</sup> of Baltimore reported four cases of massive atelectasis due to four different types of bronchial obstruction in which he demonstrated the presence of high negative intrapleural pressure, and in which he relieved the distressing symptoms by introducing air into the pleural space on the side affected. Credit is due Wilson and Habliston for having further emphasized bronchial obstruction as the causative factor, for calling attention to the resulting high negative intrapleural pressure and its important rôle in the production of the characteristic symptoms and signs, and for demonstrating the practical therapeutic value of artificial pneumothorax in the relief of distressing symptoms in

practically all cases, and as the most important contributing factor toward the ultimate cure of many cases. This will receive further consideration under Treatment.

*Diagnosis* While the clinical features, including the physical signs, are quite characteristic and uniformly present and while a number of cases are being reported, it is reasonable to believe that many cases go undiagnosed because certain members of the profession are not as yet familiar with the clinical picture and the phenomena which give rise to the symptoms and signs. It is the author's opinion that all diagnosed cases should be closely studied and reported with the hope of gaining additional knowledge, and for the purpose of widely disseminating the knowledge already at hand. Especially should the authenticated facts with reference to diagnosis be widely published. These facts may be stated briefly as follows. There may be a history of a predisposing bronchitis, a pulmonary hemorrhage, or the aspiration of a foreign body. The knowledge of aneurysm, new growths or any other intrathoracic pathology which might cause bronchial occlusion, either by pressure from without or obstruction from within the bronchus should be taken into account. Trauma and surgical procedures are to be considered as predisposing factors.

The first symptoms are usually a rise of temperature, seldom above 101 to 102 degrees, and acceleration of the pulse and respiration. These are soon followed by pain in the chest and respiratory distress. The latter symptoms may become so acutely obvious that they suggest impending "catas-

trophe," a term first employed by Lee<sup>18</sup> Such a sequence of events should immediately cause the attending physician to "think massive collapse"<sup>19</sup>

The physical signs must necessarily vary with the extent and degree of collapse and the presence or absence of compensatory emphysema

In a typical case, the physical examination should elicit the following: Inspection reveals the anxious expression, the rapid respiration and cyanosis, and in some cases, cough with mucoid expectoration. The thorax on the affected side is relatively immobile with apparently some retraction of the chest wall, and in individuals with thin chest walls, the interspaces may be depressed and Litten's shadow may be absent or diminished. On the contralateral side expansion may be exaggerated, and the chest wall relatively prominent because of compensatory emphysema. The apex beat may be visibly displaced toward the side affected and its rate noted. Deviation of the trachea in the same direction may also be seen in some cases. The head may be inclined toward the affected side and the corresponding shoulder depressed, accentuating the concave line on that side of the body.

Palpation may confirm the changes in respiratory excursion, cardiac and tracheal displacement, and in most cases vocal fremitus will be absent or diminished over the collapsed lung.

Percussion usually reveals marked dullness over the area involved and increased resonance over the sound lung varying with the degree of compensatory emphysema. The displacement of the heart can usually be determined and the high position and partial fix-

tion of the diaphragm may be demonstrated.

Auscultation varies with the cause of obstruction and the degree of collapse. In well established cases there is usually an absence of breath sounds or a distant bronchial or bronchovesicular sound over the affected area. Under such conditions the whispered or spoken voice is correspondingly absent or distant. There is usually an associated bronchitis, consequently, if breath sounds are heard at all, rales are apt to be present. Overlapping emphysematous lung tissue may modify the auscultatory sounds. The location of the heart sounds may help to determine the displacement of the heart. The characteristic cardiac displacement toward the affected side is the most significant of all the physical signs, and in the absence of chronic deforming pulmonary conditions such as fibroid phthisis with adhesive pleurisy which may grasp the heart in its retractile meshes, it should be considered pathognomonic.

As may be seen by the above recital of physical signs, the diagnosis should not be difficult. After becoming fairly familiar with the clinical description of the condition, one could explain failure to diagnose a well pronounced case only by admitting the truth of Jenner's famous aphorism, "Our mistakes are due to want of examination rather than to want of knowledge."

The x-ray is a valuable aid to diagnosis in that it confirms practically all the above physical signs, and for those who are careless or untrained in bedside methods, it may be the means of making a definite diagnosis. It immediately reveals the displacement of

heart, trachea, and diaphragm, and shows marked density in that portion of the lung involved

*Differential Diagnosis* Many physicians who are not familiar with massive collapse and the principles involved in its production are apt to confuse it with therapeutic collapse by means of artificial pneumothorax or with spontaneous pneumothorax. In some respects spontaneous pneumothorax and massive collapse are similar. The sudden onset with pain in the chest, fever, dyspnea, rapid pulse and cyanosis may be found in both. Yet in many respects they are directly opposed to each other. In massive collapse the lung is atelectic because of bronchial obstruction and absorption of air. Negative pressure is created in which the pleural space participates. By virtue of this negative pressure the heart, trachea and diaphragm are displaced toward the collapsed lung in an effort to obliterate the vacuum. Pain and dyspnea are probably due to the displacement of these structures. In pneumothorax, the lung is collapsed because of pressure from air in the pleural space which may produce a high positive pressure. The heart and mediastinal structures are pushed away from the affected side and the diaphragm is displaced downward. Pain, dyspnea and cyanosis are the result of positive pressure and the displacement of the heart in the opposite direction with the added influence of infection of the pleural surfaces and the early development of fluid in the pleural space.

The physical signs in the two conditions are so obviously different that it seems unnecessary to enumerate

them. If by any chance the examiner should be in doubt, he can rely on the x-ray for differential diagnosis.

Pneumonia is also to be differentiated from massive collapse. Pneumonia with extensive consolidation may easily be mistaken for massive collapse, or vice versa. Since massive collapse has been recognized as an occasional complication of pneumonia,<sup>20</sup> the diagnosis is rendered even more difficult. The absence of displacement of the heart, the characteristic physical signs of pneumonia, the higher fever, the bloody sputum and the higher white cell count will help to make the diagnosis of pneumonia.

Pulmonary embolism does not displace the heart, and is not apt to be diagnosed as massive collapse, no doubt, however, massive collapse is occasionally diagnosed as pulmonary embolism because the clinical picture of collapse is not generally appreciated, and because the onset in both conditions is sudden and singularly dramatic with the pronounced respiratory distress and cyanosis.

Acute heart failure from any cause, in the early course of its development, may be confused with massive collapse but a discriminating study of the history and physical signs will soon make the diagnosis clear.

Pleural effusion is seldom diagnosed as massive collapse but the reverse does undoubtedly happen as attested by dry taps and subsequent history. Bearing in mind the clinical picture of massive collapse there should be no difficulty in distinguishing the two conditions. The history of pleurisy with effusion, the absence of retraction of the chest wall, the smoothed out interspaces, the

displacement of the heart toward the sound side, the flat percussion note over the fluid with its curved line marking the upper limit of dullness and the presence of Grocco's triangle should make the diagnosis easy

A family physician recently told me about a case in which he attempted aspiration of fluid from the pleural space, and much to his surprise, he failed to find fluid but observed a pronounced pull on the piston of his syringe. He finally withdrew the piston and permitted air to slowly enter the pleural space through the needle, which he controlled by placing his finger over the barrel of the syringe through which the negative pressure was manifested by a decided suction on his finger. To his great satisfaction his patient was perceptibly more comfortable, and after repeating the procedure two or three days in succession complete relief was obtained and the patient recovered. This case was reported to me only after I had placed in the hands of this physician Doctor Habliston's paper on massive collapse. After reading this paper a full realization of the true condition dawned upon him in a Pullman car several months after his accidental therapeutic success. This is a good example of the diagnostic light which is sure to accompany a clear conception of the clinical manifestations of this condition.

*Treatment* The treatment of massive collapse, to be successful, must ultimately result in the removal of the bronchial obstruction. Even the symptomatic treatment is best accomplished by mechanical means rather than by drugs. As stated above, the negative pleural pressure initiates practically all

the symptoms and signs and the relief of negative pressure is the first indication regardless of the cause of obstruction.

If this can be accomplished after the method of Sante,<sup>1</sup> by rolling the patient back and forth on the unaffected side, all well and good. If the patient's condition will permit, this method may be tried with the hope of relieving the obstruction while preparations for other therapeutic measures are under way. However, it appears that Sante is over-optimistic when we consider the mechanism of well established massive collapse. If this method of treatment does not result in prompt relief, artificial pneumothorax should be induced. It has been successfully employed by Habliston<sup>17</sup> and Ashbury,<sup>22</sup> and no unfavorable results have been reported. As already pointed out, this method of treatment meets the immediate indications and favors spontaneous dislodgment of the obstructing material. If bronchoscopic examination and treatment are required, the introduction of the instrument is more safely and easily accomplished after pneumothorax and the extraction of mucous plugs, foreign bodies or the removal of new growths is facilitated by the release of the suction caused by negative pressure. The success and the safety of this method will, to a great extent, depend upon the skill and experience of the operator. The same may be said of bronchoscopic treatment. Certainly pneumothorax is as safe as bronchoscopy and should be first employed. Bronchoscopic treatment, quite essential in some instances, should be reserved for those cases in which other methods have failed, and

employed after the distressing symptoms have been relieved by pneumothorax, and after the trachea and other mediastinal structures have been restored to their normal position so the operator will not be handicapped by conditions he is unaccustomed to and which may predispose to unnecessary trauma. The possibility of pleural adhesions obliterating the pleural space and thus making pneumothorax impossible should be kept in mind. This can be determined only by the failure of an experienced operator to find pleural space.

*Case Report* On August 25, 1929, I was requested to see, with Doctors Horace Reed, William Taylor and Chester McHenry, a white female, age 13, with the following history. Upon admission to St. Anthony's Hospital on August 20, 1929, this concise but comprehensive statement with reference to present illness was recorded by the attending surgeon, Doctor Horace Reed, the patient having had no medical attention until a few hours before admission when Doctor Taylor was called.

"This patient first complained of abdominal distress and vomiting about ten days ago. On the following day she had tenderness in the right side of the abdomen and this tenderness has persisted to the present time. She has been out of bed part of the day during this time and has had fever until yesterday when she perspired profusely and her father thought she was free from fever. Following this she developed looseness of the bowels with cramps and diarrhea. Pain was controlled by an eighth of a grain of morphine given by mouth. As a result

of this medication she appeared to be comfortable but fever continued. Examination shows a large fixed tender mass in the right abdomen just above McBurney's point. Impression: Abdominal abscess from ruptured appendix."

To this statement should be added the fact that the patient had what appeared to be a common cold with an associated bronchitis coincident with the onset of abdominal pain, and she was coughing and raising a mucoid material at the time of admission to the hospital. The past history and the family history are unimportant. The physical signs of bronchitis were recorded and the physical examination otherwise was negative. Upon admission, the pulse was 120, temperature, 102, blood pressure, 96 over 60, WBC, 26,000, P 78, L 20, T 2. Urinalysis was negative except for acetone which was reported three plus. Culture from abdominal abscess showed gram negative bacilli, probably colon bacilli. After a hypodermic of morphine 1/16 and atropine 1/300, the abdominal abscess was drained. No attempt was made to remove the appendix. The anesthesia employed was combined local and gas oxygen. In thirty-six hours the temperature returned to normal. The inclination to cough continued but the cough was restrained as far as possible because of the abdominal soreness and pain. The patient's general condition was considered very satisfactory but the nurses' record shows that cough continued, and occasionally, in spite of the pain caused by effective coughing, large masses of mucoid sputum were raised. Elix terpin hydrate with

heroin was given for the cough and occasionally a small dose of morphine or codein for the cough and pain. At one o'clock on the morning of August 25th the temperature, after having been normal for three days, was recorded 101. At five o'clock, four hours later, the patient was awakened with a severe throbbing pain in the chest. The pulse was 130, temperature 101  $\frac{3}{5}$ ; and respiration, 37. A few hours later Doctor Reed examined the patient and made the following note:

"In the last few hours the patient has had a rather sudden temperature elevation and rapid respiration. The right side of the chest is retracted, the heart appears to be displaced toward the right, and on percussion, the right side of the chest is flat. Impression: Massive collapse of right lung—post-operative."

The x-ray (figure 1) confirmed Doctor Reed's findings. Consultation at this time resulted in a decision to induce artificial pneumothorax. The pneumothorax needle was introduced and the opening pressure was recorded, minus 10 minus 35, three hundred c. c. of air being introduced with a closing pressure of zero minus 20. The patient was promptly relieved of the most distressing symptoms and physical examination showed that the heart had returned to practically its normal position. X-ray of the chest made immediately after the treatment (figure 2) shows the heart and trachea in their normal relation to the other structures in the thorax. In twelve hours the pulse, temperature and respiration returned to normal, and all symptoms except the cough and ex-

pectoration disappeared. The subsequent course was uneventful. The cough and expectoration gradually disappeared, and on August 30th, the thoracic organs appeared to be normal, as shown by physical examination and the x-ray findings (figure 3). The patient was discharged from the hospital on September 3rd.

### CONCLUSIONS

- 1 The occurrence of massive collapse of the lung is relatively frequent.
  - 2 It is often diagnosed as spontaneous pneumothorax, pulmonary embolism, pulmonary infarct, acute cardiac failure, pleurisy with effusion, or pneumonia.
  - 3 With the clinical picture of massive collapse once well in mind, such errors in diagnosis should not occur since the symptoms are striking and the physical signs represent gross changes thus making the diagnosis easy.
  - 4 Displacement of the heart, trachea and diaphragm toward the affected area constitute the outstanding diagnostic feature.
  - 5 A review of the literature indicates that the symptoms and signs are due to bronchial obstruction and the resulting negative pressure following absorption of the entrapped air.
  - 6 The abnormal mechanical factors which exist as a result of this negative pressure tend to culminate in the symptom complex designated by Lee<sup>18</sup> as the respiratory "catastrophe."
- Since these abnormal factors are promptly corrected by artificial pneumothorax, this method of treatment should be employed in every case.



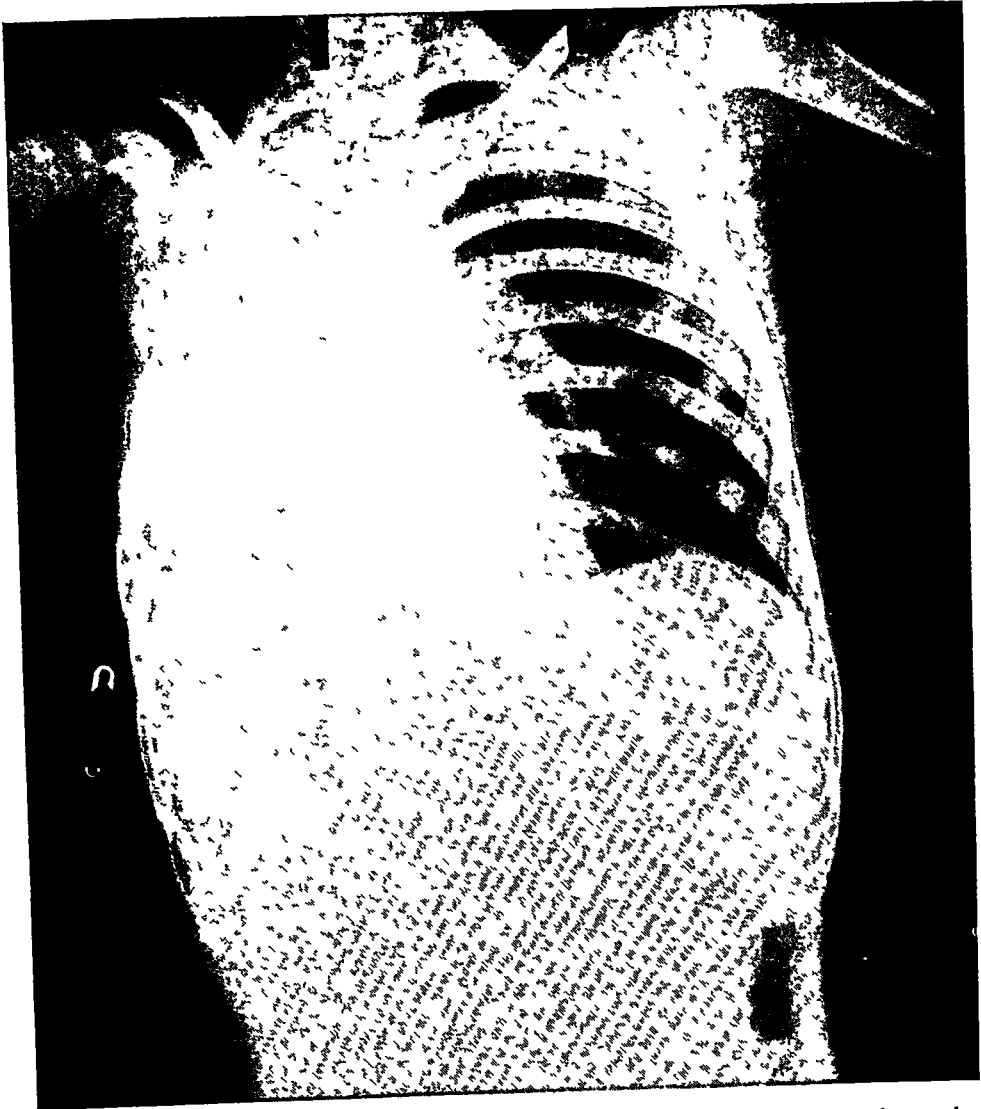


FIG 1 There is a heavy shadow of rather irregular density filling the right side. The heart is pulled over so that it occupies about the same position on the right side that it should occupy on the left. Likewise the trachea deviates far to the right, on this side the diaphragm is also very high.

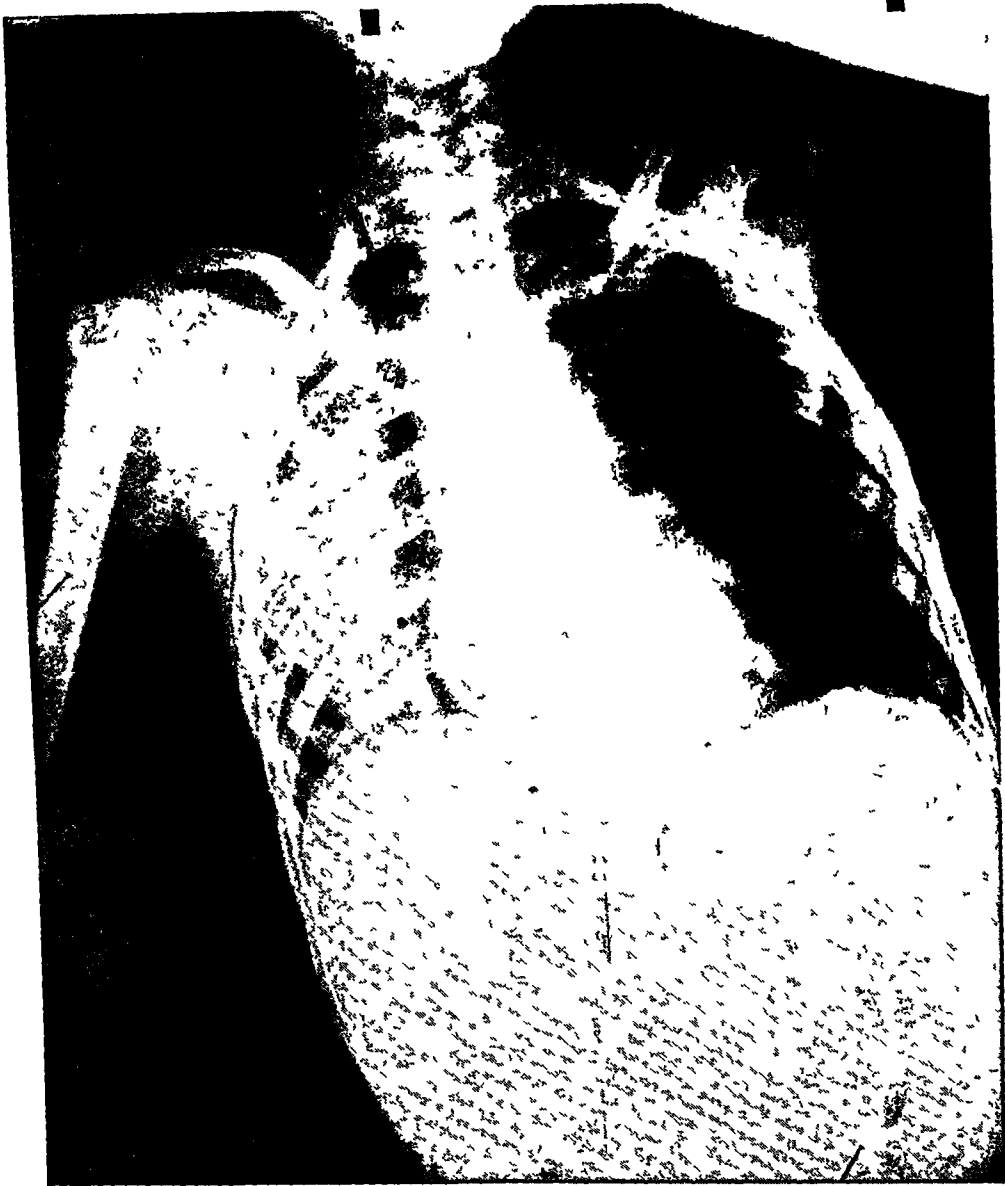


FIG 2 Represents an X-ray of the chest a few hours after the introduction of 300 c c of air. Close inspection reveals the fact that there is moderate collapse of the lung due to pneumothorax, yet the capacity is much less than in Figure No 1. However, the most striking feature in this picture is the return of the heart and trachea to their normal position and the descent of the diaphragm to its accustomed level.

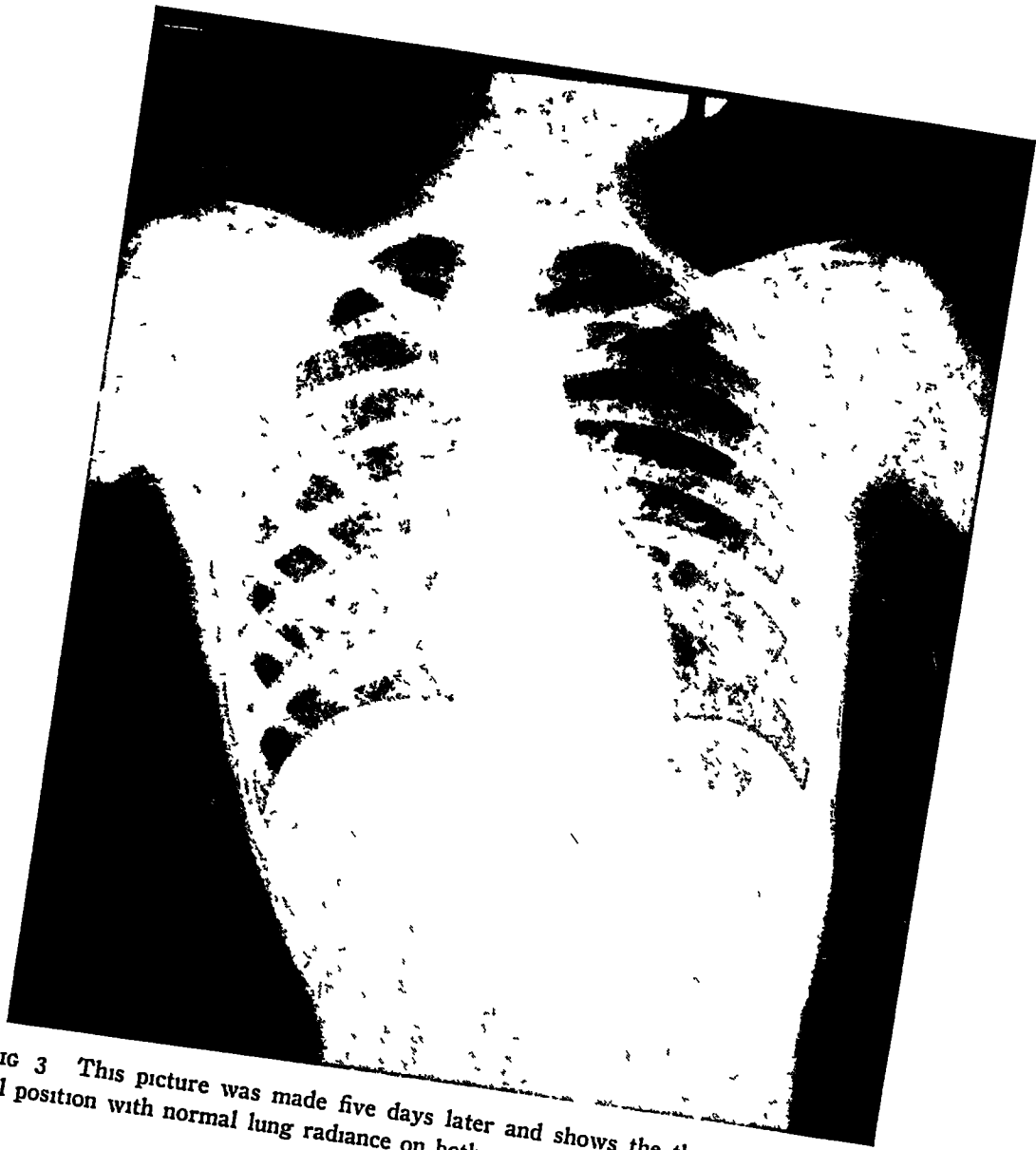


FIG 3 This picture was made five days later and shows the thoracic organs in their normal position with normal lung radiance on both sides

where spontaneous relief is not experienced after rolling the patient on the unaffected side, as suggested by San-  
te<sup>21</sup>

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# Seasonal Hay Fever Not Due to Pollen\*

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IT IS now an accepted fact that the majority of seasonal hay fever cases can be benefited by proper treatment with pollen extracts. It is also a very common observation, however, that there are many failures in such treatment. In a previous communication<sup>1</sup> I have called attention to some of the common reasons for failure to obtain satisfactory results. These were chiefly the failure to pay attention to early preseasonal, combined with seasonal treatment, individualization of pollen dosages, preservation of potency of pollen, and careful determination of the species of pollen to be used in treatment.

In addition to the above reasons for failure it has become evident that there is another important factor. Pollen hay fever may be complicated by sensitization to things other than pollen, such as orris root, feathers, animal hairs, foods, etc. These complicating factors, although in some cases insufficient to produce clinical symptoms the remainder of the year, may aggravate the condition of the mucous membranes when the pollen season arrives. In such cases treatment directed to pollen alone may prove a complete fail-

ure. Balyeat<sup>2, 3</sup> discusses this question quite thoroughly. Phillips<sup>4</sup> as well as others have discussed the importance of these secondary causes.

Not all cases of seasonal hay fever are due to pollen. A rhinitis may be due to other substances which may take on a seasonal character for various reasons. Phillips<sup>4</sup> has already emphasized this fact in connection with orris root sensitization. Spain<sup>5</sup> says that "not always, however, do patients whose symptoms are confined to a definite season of the year prove to be pollen cases." Balyeat<sup>6</sup> calls further attention to this fact.

During this summer I have observed two cases, the history and course of which illustrate this very nicely.

## CASE I

Mrs. J. L. R., a physician's wife, aged 34, consulted me on June 11, 1929, for her hay fever. Her symptoms during the season consisted of sneezing, profuse watery discharge from nose, nasal obstruction, itching of nose and eyes, and lachrymation. These symptoms have been present for eight seasons, but they have become quite marked in the last three or four seasons. The hay fever began each year in August continuing through September, with the exception of 1927 when it began in the latter part of July. She had no symptoms at the time of her visit.

\*From the Asthma and Hay Fever Clinic, Northwestern University Medical School.

She has had a few mild "colds" in winter which were not accompanied by lacrymation or nasal itching

There are no house pets. She sleeps on a feather pillow and hair mattress, and has down and hair stuffing in furniture. She has a variety of furs. She uses face powder known to contain orris root and also uses bath powder freely during the summer.

She has had a tonsillectomy in 1924 without any effect on the hay fever. There is no familial history of asthma, hay fever, urticaria, or eczema.

Skin tests made with the pollen causing hay fever in this vicinity were all negative. Intradermal tests with ragweed pollen extracts of 1:1,000 and grass pollen extract of 1:1,000 were also negative. The dry pollen of the giant and short ragweed placed in the conjunctival sac caused no hay fever reaction.

Because of slight peculiarities in her history it was suspected that there might be a sensitiveness to orris root. The cutaneous test with the latter resulted in a ++++ reaction. She was then tested completely with other proteins such as epidermal, foods and miscellaneous materials — — — — with negative results.

The patient was instructed to change her face powder to one definitely known not to contain orris root and to remove all bath powder and other cosmetics which might contain orris root. No other treatment was used.

She had followed the above direction and on October 17, 1929, she reports that she has had absolutely no symptoms of hay fever during the entire pollen season.

#### CASE II

Miss B. L., a young woman, was referred to me by an otolaryngologist on June 19, 1929, with complaints of sneezing, rhinitis, blocking of nose and lacrymation. These symptoms were marked at the time of the

examination. She says that she has had these symptoms for the last four years during June and July. At times she has had slight symptoms during April or August.

She uses face powder known to contain orris root. She does not employ any talcum powder, although there are several members in the household who do use it. Her mother has a vasomotor rhinitis. Other points in her history were of no significance.

The history was of course suggestive of grass pollen hay fever. The grass pollen as well as other pollen were negative on cutaneous tests. Intradermal tests with grass pollen of 1:1,000 were also negative. The cutaneous reaction to orris root was +++.

She was instructed to change her face powder and other toilet preparations. On June 24, five days after the first visit, she reported that she was almost entirely relieved of her hay fever symptoms. On September 11 she reported that, with the exception of an occasional sneeze, she has had no trouble since the last report.

#### SUMMARY

Two cases of seasonal hay fever are reported in which tests and subsequent therapeutic results showed them to be caused by orris root and not by pollen. The seasonal nature of these cases is to be explained by the fact that the limit of tolerance to the orris root has been exceeded only during the summer months when the use of powder is excessive. These cases are presented to emphasize the fact that in the management of hay fever patients thorough testing with pollens is imperative as well as a consideration of other factors which may be responsible for the symptoms.

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# Cavitation and Repair of Pulmonary Tuberculosis

By A N SINCLAIR, M B, C M, F A C P, *Medical Director of the  
Leah Home, Honolulu, Hawaii*

UNTIL recent years the occurrence of cavity in the course of pulmonary tuberculosis was accepted as heralding the doom of the patient

The study of serial radiographs, however, disclosing annular shadows that contracted and even disappeared awakened the observers to the possibility of cavities becoming not only healed but even obliterated with little or no evidence of their past occurrence

This was not accepted at first, such annular shadows being classified as pleural shadows, but the evidence produced by many observers has established the conviction that cavities can heal with or without leaving evidence of their past occurrence

The question that presents itself is why do some cavities heal and others do not?

The obvious answer is some individuals develop more resistance than others

Simple as such an answer appears it involves a maze of tangled paths that requires considerable thought and study to discover which one leads to the desired end

This paper is an attempt to designate these paths and correlate the mass of evidence from many sources with personal clinical experience and radiographic observations

The fundamental principles of cavity formation and then radiographic characters have been well presented by Baum, Mebel and Kane<sup>1</sup> and these will be accepted for the purpose of tracing the sequential course of tuberculosis pulmonary lesions

The success or failure of resistance to invasion by an organism depends on two factors the virulence of the organism on the one hand, and on the other upon the amount of immunity present or allergy developed (we shall not here consider massiveness of dose)

If the resistance is sufficient to overcome the virulence we shall call it a high or rising allergy or immunity as the case may be, if insufficient, a low or falling allergy, or immunity

It is here necessary to discuss allergy and immunity, as much difference of opinion exists as to their relationship

Krause defines immunity as a function of allergy and enunciates laws that make them run a parallel course

On the other hand, when we come to consider Ranke's classification of the different stages of pulmonary tuberculosis, we will find that he considers the third stage as that in which allergy has ceased and immunity has become established

As we shall see, exudative lesions are characteristic of the first and second allergic stages and productive lesions are characteristic of the third



stage "when allergy has ceased and immunity has been established"

Pinner points out that animal experimentation can not throw much light on this difference of opinion, inasmuch as most experimental animals die in Ranke's second stage<sup>2</sup>

Willis<sup>3</sup> in discussing an attempt to account for the discrepancy (according to Krause's hypothesis) between the coexistence of a high immunity and a low or apparently absent allergy refers to the fact established by Wollstein that a person after recovery from typhoid fever, or after inoculation of typhoid vaccine, may not necessarily give a good agglutination test under ordinary circumstances, yet exhibit a good Widal reaction almost immediately after a new introduction of typhoid bacilli or vaccine into the body

It may therefore be assumed, without unvarnished assumption on our part, that an individual may have a healed or non-allergic lesion, with even a temporary loss of immunity but invasion of a not too virulent organism may awaken not only allergy but an outstripping immunity, with the result that allergy is subordinated and immunity reactions become dominant. Further, without denying that healing of an allergic lesion can occur by resorption or even by restitution we may further predicate that since exudation is a lesion of allergy and productivity a lesion of immunity it is the imbalance between allergy and immunity that determines whether an exudative or productive lesion develops

We may now go on to consider the production of cavity and repair, correlating the pathological changes with the three stages determined by Ranke,

i.e. exudative, alterative, and productive

In the initial infection with tubercle bacilli (the primary infect of Ranke) there is an attempt to wall off the invading bacilli resulting in an exudative inflammation of the parenchyma of the lung, around the site of invasion

This may be successful and resorption occur. Since the infiltration is into the open spaces of the lung (alveoli etc.) the underlying structure remains intact, and such a lesion may be resorbed without injury to the lung

On the other hand, bacilli may escape to the periphery and there form new tubercles ("resorption tubercles"). These new tubercles are prone to break down and undergo caseation. As they unite with the caseating center, necrosis occurring from without in, there is thus produced a cavity with irregular walls (notched border) presenting the appearance on the radiograph of an irregular "clover-leaf" edge

There is little perifocal inflammation so that no clouded lung parenchyma is interposed between the X-ray tube and film within the boundary of the annular shadow. Moreover, as caseation and repair travel from without in, these cavities give the appearance of a sequestrum—so called "sequestrum cavity"

Further, such cavities, when small, may give no physical signs (due to normal lung tissue between them and the chest wall) producing the so-called "silent cavity"

Such cavities usually occur in the outer third of the field and below the second rib—thus being the site of election of the primary complex

In spite of the excavation of lung tissue that may occur in these cavities, it is possible to have persisting numerous elastic fibers, and it is the presence of these elastic fibers that form a basis for new connective tissue and contraction and even for reconstruction of lung tissue when the cavity heals

Should allergy be low (or late in development) the breaking down lesion may disseminate the bacilli to other parts of the lung, initiating the second allergic stage

These changes are graphically shown on chart I

Before considering what occurs in

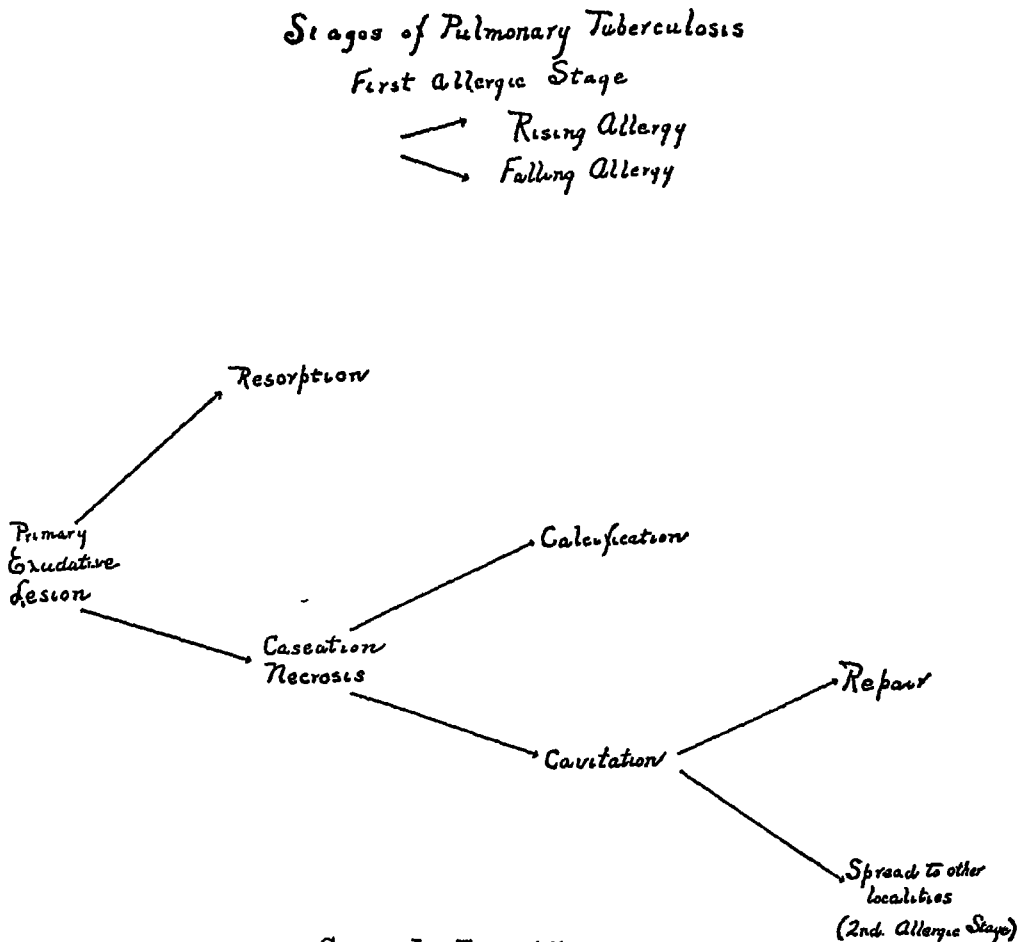


CHART I First Allergic Stage

the second allergic stage, it is necessary to refer to an observation by Koch and known as Koch's phenomenon

Koch discovered that animals already infected by living tubercle react differently to an injection of tubercle bacilli than normal animals.

In healthy animals an injection of

virulent bacilli tends to produce a generalized tuberculosis from dissemination from the original focus

In tuberculous infected animals an entirely different series of events occurs. Soon after inoculation there is an inflammatory reaction at the site of inoculation, this becomes intense

ending in necrosis and sloughing but the process does not disseminate, remaining a purely local reaction

Romer further found that if a small amount of bacilli be inoculated in these already infected animals the reaction may be so slight as to subside and healing follow—a large amount of bacilli producing extensive sloughing and death of the animal from cachexia<sup>1</sup>

Briefly summed up we may say that in a primary infection the allergy is localized, there being no barrier to generalized spread—in the secondary infection the allergy is general and this barrier while causing a more severe local reaction prevents generalized spread

Bearing in mind this distinction between localized allergy in the primary infect, and a generalized allergy in the secondary lesion, we can readily understand the pathological changes in the second allergic stage

What occurs in a secondary spread depends in a way on the number of lesions—for ease of description we will designate them as single or multiple. A spread to multiple sites, even though considerable allergy exists may overwhelm the resistance by the third factor of infection—massiveness of dose, we have then the usually fatal type of invasion (miliary tuberculosis,) which according to Korteweg and Hoeffler can occur only in allergic organisms<sup>2</sup>

When the dissemination is not so great, there is not such an overwhelming of resistance—there follows caseation and necrosis, with either extensive catacombing of the lung from a caseating or desquamating pneumonia or cavities with a fibrogenetic wall but

which require the third productive stage of Ranke to become obliterated, paralleling somewhat the second type of miliary tuberculosis of Heubschman and Arnold, as referred to by Pinner<sup>2</sup>

Such cavities seldom heal without heavy fibrotic formation (3rd stage) or spread by juxtaposition

When the lesion is single, however, there is an intense allergic reaction and a more diffused response of the tissues surrounding the secondary lesion (comparable to the more severe reaction observed in Koch's phenomenon) this is the "circumfocal inflammation" of Ranke

The allergic reaction may be so intense as to cause the lesion to pass directly into a stage of liquefaction necrosis without caseation. There is an absence of resorption tubercles about the edge, so that the annular shadow presents a uniformly smooth rounded border. These cavities may be further recognized in the x-ray film by the haziness within the annular shadow from the interposition of the inflamed lung between them and the chest walls. They are not confined to the outer third of the field—occurring almost anywhere, and furthermore, due to the absence of resorption tubercles, they may exist without tubercle bacilli in the sputum

This cavity (the pyoid cavity) offers two extremes in the final outcome. The allergic reaction may be so severe that allergy defeats its own ends—there may be a violent diffuse necrosis spread throughout a part of the lung. On the other hand resorption or repair is more easily secured than in either the primary or tertiary stage

These cavities may also have bands of the resistant elastic tissue to aid contraction and repair, and there being no broken down resorption tubercles at the edge, the walls of such a cavity can come together evenly and smoothly and heal with the minimum amount of scar tissue, which may further contract to a more or less noticeable density on the x-ray film

If allergy, in the second lesion, is but moderately present, there is liable to occur a proliferative response rather than a pyoid cavity, as referred to by Pottenger<sup>5</sup> and due to auto-tuberculin inoculation

An increased allergy at this time may lead to resorption or repair but if allergy does not rise this proliferative response may infiltrate the lung tissue and such a condition may go on to a generalized fibroid phthisis

This condition was referred to by me in a paper on Radiographic Diagnosis of Pulmonary Tuberculosis<sup>6</sup> published in 1924

I believe this is the condition indicated on the radiograph by general minute ringed markings. One observes that these markings may occur without displacement of the central shadow, in which case they often disappear leaving the lung intact

On the other hand, if evidence of contraction appears it is an indication that the stage of proliferative response has passed and the third stage of productive lesions is fully developed

Cavitation of the secondary lesion may also occur by caseation necrosis. As the conditions of a primary lesion are approached in this process one can readily believe that this occurs because

the allergic response is too weak to produce an allergic or pyoid cavity

Should allergy remain low extensive spread or catacombing may occur but with a rising allergy there occurs a proliferative response in which case a cavity may develop with a wall of proliferation which ultimately will produce a capsule of productive tissue in the third stage.

Such cavities, therefore, do not heal by resorption or repair—they will be referred to under the third stage of Ranke

(See diagrammatic representation of changes in second allergic stage)

When the third or productive stage is reached, the healing of cavities without x-ray evidence is a remote possibility

We can readily understand this. In the productive stage there is a formation of a new tissue—this tissue does not infiltrate into the interstices of the lung structures but forces its way onward through the lung. Such a new tissue is prone to become permanent tissue showing a permanent density on the x-ray film, and if cavity has occurred this density will be visible about the annular shadow and may force its way onward to the periphery of the lung

Therefore when such a cavity heals, it heals by contraction of this fibrous tissue, the condition frequently alluded to as the closing fan, and several such lesions may lead to a cirrhosis of the lung

On the other hand, there may be sufficient immunity present to produce a productive response but insufficient in amount to produce fibrotic contraction of the lung

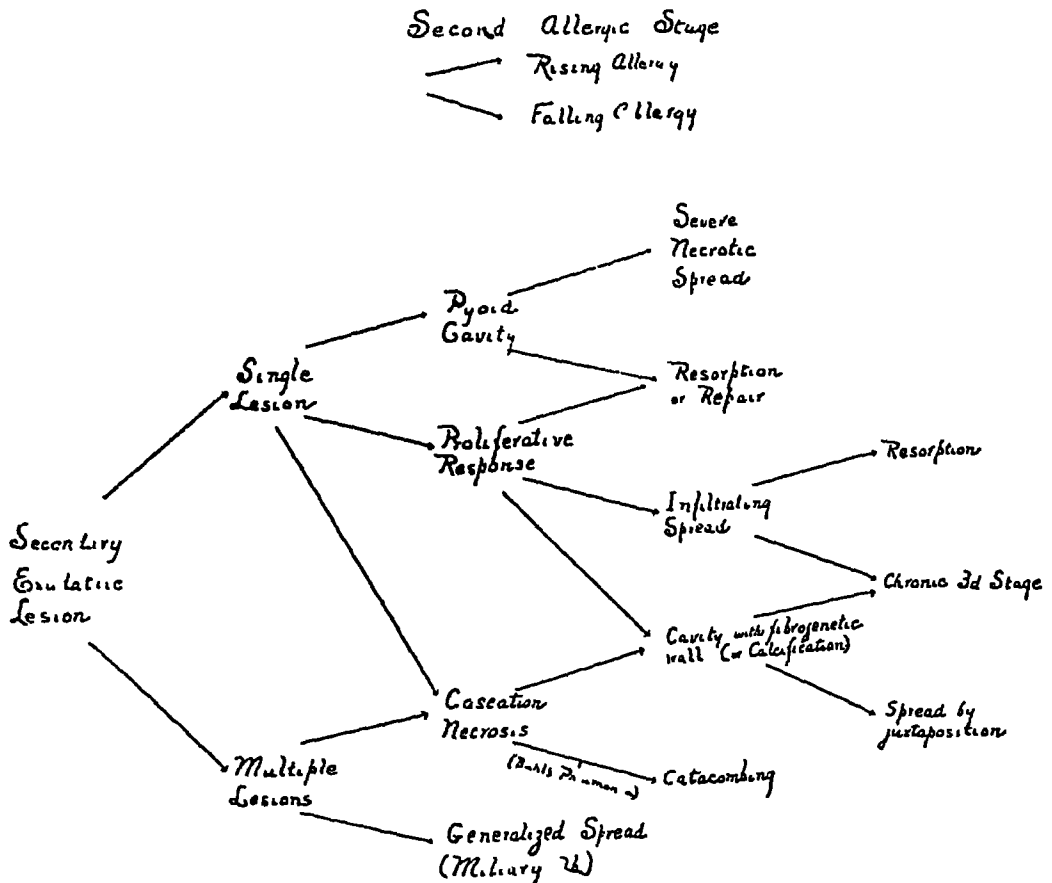


CHART II Second Allergic Stage

In such a condition cavities tend to coalesce and spread throughout the lung without apparent check—in spite of the generalized productive tuberculization—awakening no apparent reaction in the lung tissues, and even occasionally with little systematic response

Such cavities may be frequently recognized by the irregularity of their boundaries (due to the coalescence of adjacent annular shadows) as well as by the density of their borders (due to productive response)

Further presumptive evidence of third stage cavities is the synchronous presence (especially in the collateral lung) of apparently first or second al-

lergic stage lesions, due to new implantations

Rappaport<sup>7</sup> refers to Redeker's investigations in this field in regard to "subsequent infiltrations" occurring at short intervals, until one "subsequent infiltration" occurs that will not go into healing "Allergy rises to the danger line, and all previous foci, incompletely healed become surrounded by infiltrations again"

Some confusion evidently exists in the interpretation of Ranke's third stage inasmuch as in Rappaport's article this stage is characterized as possessing a lack of allergy and "by tubercles proliferating into adjacent tissues without reaction"

On the other hand, most translators refer to Ranke's third stage as being "exudative, productive, cirrhotic"

The inclusion of exudative lesions in Ranke's third stage would indicate there was a reaction between new implantations and adjacent tissues

Observations based on clinical experience and radiographic evidence warrant this conclusion

Implantations may occur in Ranke's third stage without interruption of clinical sequence (the "subsequent infiltrations" of Redeker) What then occurs depends on a phase of allergy and immunity we have already discussed

If allergy is reawakened to dominance an exudative lesion or lesions occur, which may again pass through the changes of a secondary exudative lesion—if immunity dominates the reaction, we may then have the chronic productive progressive tuberculization of Redeker, fibrosis or repair

If there has been a complete healing of a lesion in the third stage of Ranke, when immunity and allergy have been entirely lost (in which occurrence the time factor plays the most important rôle) the new lesion (or late infiltration of Redeker) will then have all the characteristics of the primary infect of Ranke

Thus the conclusion of Rappaport based on the researches of Redeker might well be the conclusion of the foregoing arguments based on the researches of Ranke

"It is therefore justly brought out by Redeker that a sharp distinction must be made between 'subsequent infiltrations' that come in the form of re-exacerbations which may be linked

to the infiltrations preceding it, and such 'late infiltrations' as are in time, and clinical sequence, far removed from any previous infiltrations 'Late infiltrations' really represent a new 'initial infiltration' out of which, in exactly the same manner as described in connection with the 'initial infiltration,' the great variety of tuberculous conditions of the lung is seen to develop; most frequently in patients between the age of forty and sixty years"

(See diagrammatic representation of changes in the third stage)

#### CONCLUSIONS

(1) The healing of cavity may occur in any stage of Ranke's classification

(2) In the primary and particularly in the secondary allergic stage healing may occur with little or no evidence of previous lesion

(3) In the tertiary stage healing being dependent on contraction of fibrous tissue (or calcification) permanent evidence remains of the healed lesion

(4) The characteristics of a primary lesion are dependent on the absence of allergy at the time of implantation, the course of the lesion is dependent upon the rate of production and amount of allergic reaction

(5) The characteristics of the secondary lesion are dependent on the presence of allergy on implantation and the course of the lesion is dependent upon the amount of allergic reaction

(6) The characteristics of lesions in Ranke's tertiary stage are dependent

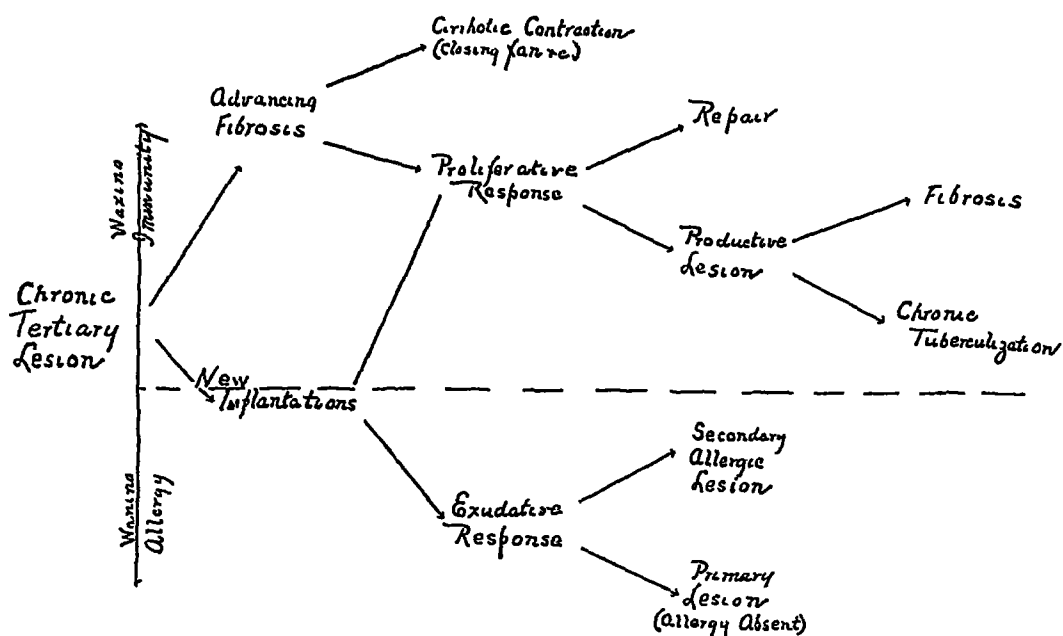
*Lesions in Tertiary Stage*

CHART III Lesions in Tertiary Stage

upon the presence of immunity and latency of allergy. The course of sequential implantations is dependent upon the imbalance between an awakened allergy and the existing or waning immunity.

New implantations in this stage are controlled by the same factors.

<sup>2</sup>PINNER, M. Amer Rev Tuberc, 1928, XVII, 601

<sup>3</sup>WILLIS, HENRY STUART. Amer Rev Tuberc, 1928, XVII, 240

<sup>4</sup>PARK & WILLIAMS, Pathogenic Microorganisms, 1924 437

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# Medical Men Who Have Attained Fame in Other Fields of Endeavor

## I. Medical Men as Musicians

By ERNEST WEINFELD, B S , M D , *New Orleans*

ONE of the most splendid tributes to the medical profession was paid by R L Stevenson, who in the dedication of "Underwoods" said, "There are men and classes of men that stand above the common herd, the soldier, the sailor, and the shepherd not infrequently; the artist rarely, more rarely still the clergyman, the physician almost as a rule. He is the flower (such as it is) of our civilization, and when that stage of man is done with, and only remembered to be marveled at in history, he will be thought to have shared as little as any in the defects of the period, and most notably exhibits the virtues of the race. Generosity he has, such as is possible only to those who practice an art, never to those who drive a trade, discretion, tested by a hundred secrets, tact, tried in a thousand embarrassments, and, what are more important, Herculean cheerfulness and courage. So it is that he brings air and cheer into the sick room, and often enough, though not so often as he wishes, brings healing." Being an invalid from early childhood and knowing the physicians well throughout his life of physical frailty, Stevenson was eminently fitted to pro-

nounce judgment upon them as a class

In the following I wish to show the medical man as standing out above the common herd in other fields of endeavor. Although we are prone to think of the medical men only in the light of their profession we do not regard sufficiently those who have attained fame in other fields. We think of the doctor of today as a busy, overworked man like all professionals or industrials in modern life with little of the leisure which people enjoyed in the ages gone by. I wish to call your attention to those who have won recognition, fame and distinction during periods of mental relaxation in other fields of endeavor, either while still meeting the demands of their chosen vocation, or after relinquishing this line of work for new fields of adventure. It is not possible to cover in any one paper the complete list of doctors who have grown famous in other fields. Some names will be omitted but enough will be grouped and classified to confirm the statement that many physicians have succeeded in other endeavors aside from their success as medical practitioners



## MEDICAL MEN AS MUSICIANS

While many articles have been written on the value of music as a healing agent, it is my purpose only to call your attention to those who have cared for music, those who became proficient performers upon some instrument, or composers, usually at the expense of what little leisure time was available. It is interesting to recall the fact that the two faculties of medicine and music have at times been united in a sufficient degree to result in their possessor's name being inscribed in both the Medical Register and various histories of music.

An early instance, according to Pits, may be found in the sixteenth century English physician, George Ethridge of Oxford who was one of the most famous vocal and instrumental musicians of the day in his own country, which at the time was in the very forefront among musical nations. (He was still living in 1585) According to Garrison, the earliest of the great European physicians to follow music as a pleasure or hobby was Felix Plater (1534-1564) of Basel who made a large collection of instruments, which still exists, played three or four of them, was an accomplished lutanist, and in his youth employed his talents in serenading his sweethearts.

The earliest extant compositions by a medical man are three songs, (dated 1596), by Thomas Campion (1570-1619), of Cambridge, England. He published Latin and English Poems as well as four books on "Ayres." He was also a theorist his "New Way of making Foure parts in Counterpart, by a most familiar and infallible Rule"

In the seventeenth century the

learned Jesuit priest, Athanasius Kircher (1602-1680) of Fulda, who was not only a medical man, but an accomplished mathematician, physicist, optician, microscopist and Orientalist. In 1640, he published at Rome, his "Musurgia Universalis sive Ars magna consoni et dissoni in X libros digesta", a huge folio of some 1,200 pages, which is a vast summary of all that was known of the theory of music in his time, including the anatomy and physiology of the ear and the throat in man and animals, descriptions and cuts of the different musical instruments, the science of harmony, the physic of the Pythagorean monochord, symphonurgy or the art of composing melodies, a history of Greek and later music, a long account of chromatics and enharmonics, the theory of time and rhythms in music, in which the rhythms of the Greek, Hebrew and other poets are considered, canon and the art of writing for different instruments. It contains notations of the songs of different birds and the sounds of animals, well executed full-page plates representing various musical instruments, and strange specimens of ecclesiastical and other music of Kircher's time.

Caspar Bartholinus (1655-1738) the Danish physician who was the son of the famous anatomist published in 1679 "De tibris veterum", a study of the double-flutes of Greece, from which the clarinet, the basset horn, the oboe, the English horn and other woodwind instruments are derived.

In the eighteenth century, John Arbuthnot (1667-1735) of England was a composer of sacred anthems. He was a friend and medical adviser

of the poet Pope and wrote "As Pants the Hart"

David Fraser Harris, M D, S M, B Sc, F R S E, F S A, Lecturer on Physiology in the University of St. Andrews, Scotland, amid his many other studies found time to become a good musician. He wrote "Saint Cecilia's Hall in the Niddry Wynd", a chapter in the history of music of the past in Edinburgh.

Herimann Boerhaave (1668-1738), of Leyden, one of the great medical teachers and theorists of his time, was perhaps the first physician on record to cultivate chamber music at his house, according to Burton. Music was his most delightful entertainment and he was not only a good performer on several instruments, particularly the lute, which he accompanied also with his voice, but a good theorist in the science, having read the ancient and best modern authors on the subjects, as appears by the lectures he gave on sound and hearing.

Richard Brocklesby (1722-97), one of the founders of military hygiene, published in 1749 an anonymous treatise recommending music for the cure of disease. The theme is as ancient as music itself—witness the familiar passages in Homer, Shakespeare and other poets, Dryden's "Alexander's Feast" and "St Cecilia".

Leopold Auenbrugger (1722-1809) of Vienna, the discoverer of percussion of the chest in diagnosis, wrote the libretto for "The Chimney-Sweep" (Der Rauchfangkehrer), an opera of Solerio which was a great favorite with Maria Theresa.

A medical man whose name is familiar to lovers of music is Thomas

Harrington (1728-1816) of Kelston, Somerset, England. His round, "Great is the Pleasure", is one of the prettiest examples of that very popular form of composition. Of his works, his hymn tune "Harrington" sometimes known as "Retirement", and his glee "Dame Duiden" suffice to carry his name to posterity. His leisure was devoted to composition when in Bath, where he established himself as a medical practitioner, being appointed Alderman and subsequently Mayor. He gained such a reputation that he was appointed "Composer and physician", on the foundation of the Harmonic Society of Bath. He wrote 4 volumes of glees and catches. Though it is by his secular works and a hymn-tune that he is best known, he also composed a dirge, "Eloi! Eloi! or the Death of Christ" for Passion Week.

William Withering (1741-99), a Birmingham practitioner who introduced the use of digitalis in heart disease, devoted his leisure hours to the flute and harpsichord.

The house of Johann Peter Frank (1745-1821), the founder of modern public hygiene, was frequented by Beethoven.

Edward Jenner (1749-1823) played both the violin and the flute.

John Ring (1752-1821) of Wincanton, England, best known as a strong advocate of vaccination in its early days, was an amateur musician and a poet, both of which faculties came into play in his "Commemoration of Handel".

Although John Hunter did not appreciate music his wife, Anne Hunter was a patron of music and wrote the words for Haydn's "Creation" and for

his charming canzonet, "My Mother Bids Me Bind My Hair"

William Kitchner (1775-1827) was born in London, educated at Eton and took his doctor's degree in medicine at Glasgow University. He inherited a fortune from his father which made him independent of exercising his profession and he devoted himself to scientific and other pursuits among which music took a prominent place. In addition to editing the "Loyal and National Songs of England, for one, two and three voices selected from original manuscripts and early printed copies in the Library of William Kitchener, M.D., London, 1823," "Sea Songs of England", and the "Sea Songs" of Charles Dibdin, with a memoir of his Life and Writings (1824)", he composed "Amatory and Anacreontic Songs Set to Music" (Solo songs, glees and catches for the Anacreontic Society, an aristocratic but not too refined musical society). Kitchener composed a musical drama under the title "Ivanhoe, of the Knight Templars", and an operetta, "Love Among the Roses, or the Master Key." He also published a book in 1821 of "Observation on Vocal Music"

Florent Corneille Kist (1796-1863) was born at Arnheim, studied medicine and practiced as a doctor at the Hague until 1825, after which he seemed to have abandoned himself almost entirely to the "Devine Art". In 1827 he founded the "Diligentia" music society, organized and presided over several singing societies. His printed compositions consist of vocal pieces for one and several voices, and a volume of variations for the flute, on

which, and on the horn, he was an excellent performer, and some larger works, such as cantatas which remain in manuscript. But it is chiefly as an organizer of musical societies at Delft, the Hague, and Utrecht, and founder of Cecilia, which at the present day remains the most important musical paper in Holland, that he will be remembered. He also wrote musico-historical works of some importance.

Sir Robert Christison (1797-1882) of Edinburgh who wrote the first treatise on toxicology in English, although self taught in music, was a good bass singer. Dr Christison, Dr Bennett, Dr MacLagan and Dr Peddie were among the first gentlemen amateur vocalists who ventured to perform publicly in Edinburgh. They sang much together and were known as the singing doctors. In making a crossing from Brighton and Dieppe in his early days Christison found that his traveling companions—two English and two Irish doctors and Schetky, a drawing master, were musical, so that he was able to improvise a nautical concert. Turner, a violincellist, Corban a violinist, Crawford a flutist, and Schetky a violincellist.

Emile Joseph Maurice Chevé (1804-1864) was born at Dowarnenez, Finistère. He wrote a complete exposition on the tonic-sol-fa and "Movable Doh" system (invented by Guido, of Arezzo (995-1050 A.D.) a monk), and profession. He also founded a music school "Methods Elementaire de la Musique Vocale," in which he taught on the new plan, and tried repeatedly, though in vain, to provoke the Conservatoire into a discussion of their respective methods. It made

considerable progress and is now allowed in the communal schools

Sir William Fergusson (1808-77), of Prestonpan, Scotland, was a very accomplished violinist

Joseph Hyrtl (1810-94) was the first and greatest teacher of topographical and regional anatomy in the nineteenth century. His father, a musician in the Count Esterhazy's band, had played an oboe under Hayden and Hyrtl, himself a chorister in his youth. He was one of the greatest medical philologists, a man to whom written and spoken Latin were as his mother tongue.

Henry Ingersoll Bowditch (1808-92) the eminent clinician was an intense lover of music. His father Nathaniel Bowditch gave up playing the flute because at one time it brought him in contact with companions whom he thought undesirable in their morals, and in consequence of which he denied the study of music to his children. He always regretted that he never learned any musical instrument. Whistling was his only accomplishment. He says, "Music has been all my life long my delight and my inspiration. I have listened (while standing three and a quarter hours in the Sistine Chapel) to the 'Miserere', and was almost persuaded thereby to become a Catholic." His wife (Olivia) was a talented singer and performer on the piano and harp, sometimes accompanying the fine voices of her sons on these instruments.

That the scientific training which a medical man receives, in the case of his having a gift for music should turn his thoughts to the theory of the art, seems but natural. Little surprise

need be felt therefore that one of the best known, if not most widely accepted, theoretical methods, the Day theory, is the work of a physician Alfred Day (1810-1849) was born in London. His devotion to the theory of the art was due to his not having been allowed in earlier life to give sufficient time to its practical side to become proficient as a performer. His father had insisted on his studying medicine and he accordingly did so in London, Paris and Heidelberg, from which latter place he took his degree. Thereafter he practiced in London as a homoeopathist. He is the best known as the author of an original "Treatise on Harmony" which after many years of study, he published in 1845. In this treatise he advocated reforms in terminology and teaching, formulated a new sort of bass-figuring to supplant the ordinary thorough-bass, and made many interesting and practical suggestions. It was revolutionary, since there was hardly any department of the subject the teaching of which the author did not propose to reform, in the words of Sir Herbert H. Parry "no other theory yet proposed can rival it in consistency and comprehensiveness" and while few authorities accept it as a whole there are probably even fewer among subsequent writers who have not been influenced by its appeal to the fundamental chord of nature and consequent orderliness and rational system.

Sir Richard Owen (1804-92) besides being an excellent chess player was an accomplished violincellist. He was very fond of the old classics but the music of Grieg and Wagner he considered as too futuristic.

Jacob Henle (1809-95) the greatest German histologist of his time and one of the greatest anatomists of all times was an accomplished musician as well as a poet and skillful artist. Beginning with the violin and eventually learning to play both viola and violincello, so that he might take any part at need in an impromptu string quartet. Henle's friendship with Humboldt, Gustav Magnus, and Felix Mendelssohn, is most interesting.

Carl Friedrich Wilhelm Ludwig (1816-95) of Leipzig, another great physiologist, was very appreciative of music, followed the Gewandhaus concerts and had chamber music at his house.

Theodor Wilhelm Engleman whose name will always be associated with Gaskell's in the physiology of heart muscle was a friend of Brahms' and to him Brahms dedicated his charming string quartette in B flat.

Herman von Helmholtz (1821-94) was not only a performer and learned connoisseur of music and musical literature, but he was the founder of musical aesthetics as a science, the author of the most exhaustive treatise on the physiological basis of tonal sensations which has ever been achieved, his "*Tonempfindungen*" (or tonal sensations). During his life he was an ardent concert goer and could have been an able critic of music.

Max Schultz (1825-74), the histologist, was a good violist, a friend of music devoting his leisure hours to the violin.

Theodor Billroth (1829-94), the pioneer of visceral surgery, was one of the greatest lovers of music. He received a thorough musical education

and was an excellent pianist. He was an intimate friend of Brahms and Hanslick, and they formed a sort of artistic triumvirate. Of this friendship Billroth's "*Briefe*" are a fascinating memorial and in his unique musical correspondence, recounts of the musical life of Vienna, the concerts, operas and oratorios, Billroth's piano duets with his friends, and the chamber music evenings, at which Brahms was of course the central figure. During his residence at Vienna (1867 till his death) the musical soirees at his house were famous. It was at Billroth's house that almost all the chamber-music of Brahms was performed before it had its first performance in public. Besides Billroth's "*Briefe*" (edited by George Fischer, 1895, 7th edition 1906) he also wrote "*Wer ist musikalisch?*" (edited by Hanslick 1896, 4th ed 1912) which is a miniature pendant to Helmholtz's treatise on tonal sensation.

Wilhelm His (1831-1904) identified the remains of Bach and had the sculptor Seffner make a bust of the great composer from his measurements, which turned out to be an admirable likeness.

Robert Cameron (1838-1876) of Logie Coldstone, Scotland, settled in Australia as a medical practitioner. He composed vocal music and numerous overtures and also served as critic for various journals.

T. L. Phipson, a physician of London, England, has left permanent memorials of his love of music in a translation of De Be Beritt's "*Methods de Violin*". His original works include "*Biographical Sketches and Anecdotes of Celebrated Violinists*".

(London, 1877) "Bellini and the Opera of La Sonnambula" (1880), "Famous Violinists and Fine Violins," "Historical Notes, Anecdotes and Reminiscences" (1896) He was a very fine musician and his powers as an executant are sufficiently proved by his having been at some time president and solo violinist of the Bohemian Orchestral Society

Alexander Ponfievitch Borodin (1834-87) was an army-surgeon and later became a professor at the Petrograd Medico-Surgical Institute He was president of the Music Society of Amateurs He was intimate with Liszt (in Weimar) and Balakirev, at whose suggestion he studied music, of which he was passionately fond He became a foremost exponent of the neo-Russian musical cult His works comprise a 4-act opera, "Prince Igor" (posthumously finished by Rimsky-Korsakov and Glazunov), 3 symphonies, symphonic poem, "Dans les Steppes de l'Asie Centrale," scherzo for orchestra, 2 string-quartets, string trio, piano quintet, piano pieces and songs

Bernard Naunyn (1839- ) the eminent clinician at Strassburg was a man of widest culture, especially in music He overcame a great deal of prejudice and opposition among the Alsatian population on account of his austere demeanor, through his attractive chamber music evenings, which came to be important social functions in the city His wife was a talented singer

Julius Jensen, the alienist, also had a talented wife, and was often seen with "Notenhefte" under his arm at concerts.

Ludimar Heilmann, Julius Jacobson Wilhelm Ebstein, Karl Kahlbaum, the psychiatrist who described hebephrenia and katatonia were all musical, sometimes giving concerts at home

Duke Karl Theodor of Bavaria, who became a well-known ophthalmologist, was musical and played in an orchestra

Alfred de Baiy, an assistant of Flechsig at Leipzig, was at once professor of psychiatry and a prominent tenor at Bayreuth and Munich

Christian A Herter (1865-1910) of Glenville, Connecticut, who was founder of the Journal of Biological Chemistry and Jacques Loeb (1859-1925) who was head of the Department of Experimental Biology in the Rockefeller Institute were excellent musicians

John Cohnheim Hemmeter (1863- ) is the composer of a cantata for male chorus and full orchestra, "Hygeia" which he dedicated to Professor William H Welch He investigated the physiologic and anatomic foundations of piano technique and of vocal tone production I may add that Hemmeter is the author of the first complete work in the English language on diseases of the stomach and his "Diseases of the Intestines" (2 vol, 1901) is the only complete work on this subject in the English language Hemmeter discovered that the x-ray could be used for studying abnormal conditions of the digestive tract (1896) and also that it was possible to investigate the stomach contents directly by the introduction of tubes, and also to pass tubes in the duodenum

Sidney Kuh (1866- ) the neu-

rologist and psychiatrist, D'Orsay Hecht, and Gustav Langmann, have been capable performers or even composers

Arpad G. Gerster (1848- ) in his "Recollections" says: "What musical training I managed to acquire has yielded me much pleasure amidst the cares and fatigues of professional life, for discernment and appreciation of good music are of greater importance for the non-professional lover of the art than technical facility"

Nicholas Steer, a schoolmate of Gerster, held gatherings in his rooms while studying medicine in Vienna, for a select coterie of students eminent for their scholarship or as musical connoisseurs. Steer showed a decided musical talent very early and soon became a pianist, above the level of dilettantism. During his connection with Billroth's Clinic this accomplishment was honored by frequent invitations to play four hands with the Professor, also a splendid pianist.

A string quartette was organized under Ernst Schwessel's leadership which performed at Gerster's house every four weeks during the winter months. With occasional interruptions these reunions continued during fourteen years. The membership varied somewhat but among its more permanent constituents were, Schwessel, first violin, Dr. Fred Kammerer, 'cellist, Dr. Felix Cohn, violist, Donaldson, 2nd violinist. Later Ulysse Buehler, the pianist, took active part in the chamber music. He played with the Dannreuther Sunday Quartette at Dr. Knight's, the continuation of Dr. Sands' Quartette Club. The quartette repertoire was varied by trios, quin-

tettes, and occasionally a duo. Bach's concerto for two violins and piano in D minor was invariably played once a year.

In 1884 John White played several of Bach's organ compositions during a series of recitals at the Old Chickering Hall. They created such a profound impression that under the stress of his emotions Gerster bought an organ. He practiced on the organ of All Soul's Church twice weekly for two years and later said, "Although technical accomplishment was denied, thorough acquaintance with Bach's organ works made my organ practice more than worth while." To attest Gerster's love for music during the year October 1872-October 1873, he attended 62 operas.

In the Life of Elie Metchnikoff (1845-1916) his wife (Olga) speaks of him as a great lover of music. "The last examinations took place in the spring of 1862. It happened to be the Italian Opera season and Elie could not resist the temptations offered him by music. In order to make up the time, he often had to work the whole night long at the cost of severe fatigue." During his stay in Germany, music was the young man's only recreation. He did not play any instrument, his parents discouraged him yet he certainly had a natural talent for music, which he passionately loved. He could only whistle, but with that feeble means succeeded in reproducing complicated compositions. Having assiduously attended excellent concerts, he had made himself thoroughly acquainted with classical music, and Beethoven

and Mozart always remained his favorite composers

Fritz Kreisler, as well as many other well known musicians, studied medicine

The Berlin Medical Orchestra has as practicing members only physicians, even foreigners are accepted As honorary members the association admits contributors and patrons The rehearsals were held in the Kaiserin Friedrich-Haus Each year a charity concert is given, the profits of which are for the benefit of the widows and orphans of deceased physicians. The association had about sixty members, among whom was Professor His, the director of the first Medical Clinic, who was a violin virtuoso

Vienna and Paris both have similar medical orchestras

An orchestra composed of physicians and a chorus, likewise of physicians, gave a concert in Berlin The program included Mendelssohn's "Walpurgis-

nacht", Bach's 'Third Concerto and the Bach cantata, "Gott der Herr ist Sonn'und Schild"

An orchestra of eighteen pieces has been organized by the secretary of the Summit County (Ohio) Medical Society, Dr Alexander S McCormick The players are all physicians except the drummer and a saxophone player, who are the son and nephew, respectively, of physicians

There is an orchestra composed entirely of physicians in Newark, New Jersey, which at present comprises eighteen members and performs at medical functions

Professor Janos Bokay, director of the Pediatric Clinic of Budapest University, an ardent musician, and president of the Medical Philharmonic Club, commemorated the centenary of Beethoven's death by reading to the medical society an excellent and most interesting paper entitled "The Deafness, Last Illness and Death of Beethoven"



## Editorials

### *THE ONLY HUMAN VERTEBRATE PARASITE*

For more than a hundred years travellers and explorers returning from the valley of the Amazon have brought back the strange story of a fish alleged to have the extraordinary habit of entering the human urethra, in both male and female bathers, particularly when passing urine while bathing. The unfortunate victim of such a remarkable accident, particularly the male, finds himself in a most serious predicament, for this tiny fish, once engaged in the urethra, fastens itself there through the erection of spinous processes on its gill covers, and can be removed only by means of a most serious operation, amputation of the penis. The stories have it that both men and women bathers in the Amazonian headwaters protect their genitalia, while bathing, by means of various coverings made of cocoanut shells or bark. If these stories are true, great scientific and medical interest attaches to this fish and its peculiar habits, since it would be the only known vertebrate parasite of man. Dr E W Gudger\*, of the American Museum of Natural History, has for many years been collecting the accounts of this alleged habit of the

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\*On the Alleged Penetration of the Human Urethra By an Amazonian Catfish called Candirú. American Journal of Surgery, N S, Vol VIII, p 170

Candirú, and has just published these data, together with what is most probably the true explanation of this long alleged phenomenon. The first account is that of Martius, who tells the story in his preface to Spix and Agassiz's "Selecta Genera" (1829). He says. "Concerning another fish which is also dangerous to man, I ought to add some things. The Brazilians call this fish Candirú, the Spaniards living in the province of Maynas (Peru) name it Canero. By a singular instinct it is incited to enter the excretory openings of the human body when it can get at those parts in those who are bathing in the river. With great violence it forces its way in, and desiring to eat the flesh it unfortunately brings danger to human life. These little fishes are strangely attracted by the odor of urine, and consequently the dwellers in those parts when about to go into the river Amazon, in whose bays this pest abounds, constrict the prepuce with a string and refrain from urinating." In 1831 Martius again refers to this matter in the third volume of Spix and Martius "Reise in Brasilien" as follows. "A species of this genus, the Candirú of the aborigines has the habit of entering with great impetuosity and rapidity into the external openings of the human body. It thus brings about a most painful and dangerous accident since it stretches out its fins, and can-

not be gotten out save with great difficulty. The odor of man's excretions appears to attract the little fish, and the Indians therefore advise that while in bathing none of this excretion be passed, and that this particular organ be covered carefully." The next mention of the Candirú occurs in the writings of Poeppig (1836). In a footnote he says that "The fresh juice of the Xagua is rightfully claimed to be the surest means of killing and getting rid of those two-inch long little fishes which slip into the outer openings of the bodies of careless bathers and bring about the most frightful accidents.

The attack of such a fish in such a manner is such an extraordinary thing that one can scarcely believe it. In Yurimaguas I myself have been an eye-witness of such a case. An Indian woman, after the penetration by a Canero into the vagina, suffered such frightful pain and loss of blood that she was given up to die. However, after both internal and external applications of Xagua, the little fish was gotten out and the woman came through alive." Mention of this fish and its habits was made in 1840 and 1841 without adding any actual facts to the case. In 1855 Castelnau described a little siluroid fish, as a new species from the Araguay and Amazon rivers, of which he makes the following extraordinary observation: "This species is, on the part of the fishermen of the Araguay, the object of a most singular prejudice. They claim that it is very dangerous to urinate into the river, because, they allege, this little animal launches itself out of the water and penetrates the urethra by ascending the length of the liquid column."

When Reinhardt (1859) discovered a small, slender catfish provided with retrorse gill-cover spines, living in the gill-cavities of a huge silurid of another family, he sought from its habits to connect his fish with the Candirú. He regarded it as highly probable that if not identical with his species, it must be one closely related to it. During the next two decades the story of the Candirú and its alleged penetration of the urethra is repeated by most travelers in Brazil, although none of them had seen a case confirmatory of it. The story told with so much circum-spection and detail by the natives to these various explorers apparently made most of them believe that a real danger existed. In 1897 Dr G. A. Boulenger exhibited specimens of fish collected by Dr J. Bach in the course of an exploration of the Rio Jurura, a southwestern tributary of the Amazon, with the following data concerning the habits of the fish: "The Candyrú, as the fish is called, is much dreaded by the natives of the Jurura district, who, in order to protect themselves, rarely enter the river without covering their genitalia by means of a sheath formed of a small coconut shell, with a minute perforation to let out urine, maintained in a sort of bag of palm-fibers, suspended from a belt of the same material. The fish is attracted by the urine, and when once it has made its way into the urethra, cannot be pulled out again owing to the spines which arm its opercles. The only means of preventing it from reaching the bladder, where it causes inflammation and ultimately death, is to instantly amputate the penis, and at Tres Unidos, Dr Bach had actually

examined a man and three boys with amputated penes as a result of this dreadful accident Dr Bach was therefore satisfied that the account given of this extraordinary habit of the 'Candyrú' is perfectly trustworthy" In 1898 Jobert wrote an article in which he gave his own observations and critically discussed the whole matter Although expressing much doubt as to the truth of the various stories, Jobert does think there is some foundation for these allegations, and had personal experience while in bathing near Pará, by receiving scarifications on his body from some small fishes On showing these wounds to Dr Castro, a physician of high standing in Pará, and a man much interested in natural history, Jobert was assured by him that his wounds were made by the fish and convinced him of his firm belief in the possibility of urethral penetration by the same "Because I have myself extracted from the urethra of a negress a little Candirú which had penetrated during micturition while bathing in the river The patient experienced cruel suffering, for since I had to drag the animal out the extraction was difficult, and the mucous membrane was lacerated" Krause (1911), Woodroffe (1914) and Rudolf von Ihering (1914) all appear to be convinced of the truth of the allegation as to the penetration of the body openings by the Candirú, although not possessing any first-hand knowledge of its actual occurrence Dr C H Eigenmann, the outstanding authority on South American fishes, gives an extended account of the Candirú stories, and indicates plainly that he had full belief in the oft-repeated

tale, to the extent that he established a new genus of Candirú, *Urimophilus erythrurus* The last published account of this parasite is by Paul Le Comte (1922), who says of the Candirú "The worst is that it penetrates sometimes into the anal and urinal apertures of men and women bathers, and there erects the terrible spines which oppose all efforts to extract it, thus causing terrible disorders if it is not gotten out with the greatest care I have personally known already three cases of this curious accident" W E Pearson, one of Eigenmann's students, adds a hearsay instance of the penetration of the vagina by a Candiru in the Rio Beni region where it seems that females alone are attacked Gudger marshals the evidence to and for the Candirú, as a lawyer would in court, and after a careful analysis of the habits of these fish he is able to show a steady and unbroken gradation of habits leading to endoparasitism in certain forms in those species loosely called Candirús The secretive action of these cat fish, the fact that they are colorless or translucent, their carnivorous habits, and the definite establishment of ectoparasitism in some species make it not a far cry to the establishment of the habit of semi-internal living in the branchial chambers of the host, and the development of an instinct to enter the external openings of the body From a number of observers it has been definitely determined that various members of the catfish family are carnivorous, and that they will attack, by attaching themselves to living fishes and mammals, and even to man himself Muller writing from Wallis' notes (1870)

says of the Candirú of the Huallaga that. "It is a formidable plague for bathers, a species of blood sucker indeed which with incredible powers of swimming goes to the body and inflicts a cupping-glass-like wound, and when it has succeeded so that it holds itself fast to the body, it spreads out in the wound a bundle of needles whereby, as if with barbs, it clings so tightly that only by a painful operation can it be separated from the body" Thus is ectoparasitism definitely established, and taken in connection with Jobert's experience at Pará, there can be no doubt that there certainly exist in Brazilian waters fishes of small size that are capable of attacking men and drawing blood. Of the ectoparasitism of these small catfish upon larger fish there is abundant evidence in the literature. Endoparasitism in a fish of this family was first established by Reinhardt (1859) in his discovery of *Stegophilus insidiosus*, and was confirmed in 1911, by Pelligrin, whose descriptions make it clear that this fish is a blood-sucking parasite adapted for penetrating between the gills of large fishes, and that it, or a near relative, was Jobert's assailant. Their gill penetration and blood-sucking habits have undoubtedly grown out of their primal ancestral habit of creeping under objects and into cavities for protection and for animal food. It has been conclusively shown that the more specialized catfish are attracted by flesh and blood, that they will attack and scarify,

not only the gills and bodies of mammalian beasts, and that they will also puncture the skin and suck the blood of man. They are attracted, particularly to man, by the odorous secretions given off by the body. It does not seem too much to think that they would be attracted by the most abundant, and possibly the most tropic of all, urine. The evidence as set forth seems strongly to indicate that the Candirús are tropic to urine. Gudgee says that during the many years in which he had been collecting accounts of the alleged penetration of the human urethra by the Candirú, he had been very skeptical on the subject. In medical literature he has found 74 cases of invertebrate penetrations and voidings of the human urethra. If certain elongate and sinuous invertebrates do penetrate the human urethra, do the elongate and sinuous Candirús penetrate also? From all of the known accounts by explorers and naturalists, from the persistent widespread local belief and the universal use of protective contrivances by the natives in the region where these fish are found, and the testimony of competent eye-witnesses, Gudgee concludes that this evidence is sufficient to convince a jury in a court of law, and that he cannot withhold his belief in the penetration of the human urethra by the Candirú, a slender catfish found in Amazonian waters. This fish is therefore to be regarded as the only known vertebrate parasite of man.

## Abstracts

*Cardiac Pain* A Consideration of Its Nosology and Clinical Associations By ROBERT L. LEVY (Amer Heart Jour, 1924, Vol IV, p 377)

Pain in the region of the heart is a common complaint. Its significance for the patient may be slight or grave, but since Heberden's time, the occurrence of such pain has come to carry with it, in the minds of the laity, and in the judgment of many physicians as well, the suggestion of sudden death. The "disorder of the breast" described by Heberden, in the light of increasing experience, has proved to be the symptomatic manifestations of many pathological states. The perpetuation of the name originally given to the condition, and the concept of angina as a clinical entity, has resulted in confusion and disagreement as to its precise meaning. It is therefore suggested that the term "angina pectoris" be abandoned. Correlation of clinical and pathological data has demonstrated that cardiac pain may be associated with a variety of structural and functional changes. Pain resulting from disturbances in the region of the heart is best described as *cardiac pain*. In making a complete cardiac diagnosis, this should be qualified by the statement as to the probable structural and functional changes with which the pain is associated. Further knowledge concerning the mechanism of pain production may point the way to a more precise terminology. The conception of pain as a symptom will make for better diagnosis, for rational therapy, and for more accurate prognosis. If pain be regarded as an expression of a disturbed functional or structural state, therapy must be directed toward correcting or alleviating the basic disorder. This is the plan usually followed in medical or surgical practice, it is the logical procedure when the pain originates in the heart. Levy is pessimistic as to the treatment of cardiac pain by the attempt

to obtain symptomatic relief through surgery of the cervical sympathetic. The results of cervical sympathectomy so far have been variable, and on the whole, disappointing. It is his opinion that this operation will prove to have a very limited field of usefulness. He regards the paravertebral injection of alcohol into the posterior nerve roots as an uncertain procedure, unaided by visual guidance and not without hazard. The relief afforded in some instances may well be due to blocking of cutaneous impulses, and while prompt in some cases, may be only temporary.

*Urobilinuria in Vomiting of Pregnancy* By VICTOR JOHN HARDING and H. B. VAN WYCK (Jour of Obst and Gyn of the Brit Empire, Vol 36, No 3)

In a previous paper these workers discussed the serum protein values in vomiting of pregnancy. They stated that, in general, a high value for serum protein meant a favorable prognosis, and a relatively easy treatment. But in a few cases, although the ultimate outcome was successful, the course of treatment offered difficulties. Their final study leads them to conclude that the long series of observations carried on by them shows that four factors must be considered in the treatment of vomiting of pregnancy — starvation, dehydration, hepatic dysfunction and neurosis. Except for the latter, the use of fluids and glucose usually form sufficient therapy. In occasional cases, the hepatic function fails to be restored coincidently with or immediately following the overcoming of the dehydration. In some cases they recommend the feeding of a higher number of calories in the form of a large amount of carbohydrate and a little protein. While the factors can thus be stated in general terms, the extent to which each is present in individual patients will vary. Urobilinuria is present in about 80 per cent of all

cases of nausea and vomiting in pregnancy admitted to the wards of the Toronto General Hospital. On resumption of food after dehydration has been removed the urobilinuria generally disappears. Some cases show a persistent urobilinuria. Generally a persistent urobilinuria is to be correlated with a slow recovery from vomiting of pregnancy. In some cases of persistent urobilinuria it has been found necessary to feed by means of duodenal tube.

*Action of Ephedrine and Pseudoephedrine Upon the Bronchial Muscle* By C PAK and T KING (Proc of the Soc f Exper Biol and Med, January, 1930, p 253)

These workers studied the peripheral action of ephedrine and pseudoephedrine on rabbit bronchial muscle, using their modified method of the isolated lung perfusion described by Sollmann and Van Oettingen. The response of the bronchial muscle varied with the dosage. Perfusion with highly diluted concentrations, such as 1:1,000,000 to 1:5,000,000 in 6 experiments produced a definite bronchial dilatation, and the effect of 1:1,000,000 was more distinct than that of the more dilute solution. Comparing this effect with the action of ephedrine on the circulation and other smooth muscles the bronchial dilation is probably a sympathetic reaction. Perfusion with moderate concentrations of ephedrine, namely, 1:10,000 to 1:200,000 in 7 experiments uniformly caused bronchial constriction, and the effect of 1:10,000 was stronger than that of 1:100,000. In 4 experiments, atropine 1:400,000, perfused for 6-10 minutes previous to ephedrine had no influence on the bronchial constricting effect of ephedrine. In this instance the broncho-constricting effect of ephedrine is probably a muscular effect, and its sympathetic action is apparently not present. Perfusion with high concentrations, i.e., 1:200 to 1:2,000 in 9 experiments caused either marked constriction (4 cases), or marked dilatation of the bronchioles, depending on the condition of the bronchial muscle and its sensitivity to drugs. The constricting effect was more pronounced than that from moderate concentrations of ephedrine. The marked dilatation may be due to direct muscular depression, as the subsequent injection

of barium chloride produced no effect. The action of pseudoephedrine on the bronchial muscle is similar to that of ephedrine. Concentrations between 1:1,000,000 and 1:100,000 in 5 experiments produced bronchial dilatation in sensitive bronchial preparations, but no effects in insensitive ones. The perfusion with 1:10,000 and with 1:2,000 each in 2 experiments produced a regular distinct bronchial constriction, and the constricting effect of 1:10,000 was apparently stronger than the same concentration of ephedrine. Pseudoephedrine seems to be more musculotropic than ephedrine. These workers conclude that ephedrine is a sympathomimetic and musculotropic drug, and this fact confirms further the observation of Pak and Read on the blood pressor action. The divergent results obtained by different workers are possibly due to dissimilar dosage, one may have used larger doses in which the sympathetic action was overpowered by strong muscular action, or, on the other hand, small dosage may have been used, which produces a pure sympathetic effect.

*Krebsantikörper bei Krebskranken* By I. KIRZFELD and W. HALBER, with the clinical cooperation of M. Flockstrumpf and J. Kolodziejski (Klin Wochenschr, February 22, 1930, p 342)

These workers succeeded in demonstrating the presence of complement-binding antibodies, which react with sufficiently sensitive cancer antigens, in the sera of cancer patients, particularly in those suffering from cancer of the digestive tract, uterus and mamma. A small part of these sera gave a positive Wassermann reaction, positive lues sera react with alcoholic extracts of cancer. In explanation the conception of "Zerfallskrankheiten" is advanced, and the reaction is ascribed to the coincident presence of both specific and non-specific lipoids in cancer tissue. The sera of pregnant women also reacts with cancer antigens. The possibility is discussed that in the latter case there are anti-bodies produced against substances which occur during embryonal growth, and that these substances in cancers and embryos are identical or related. In this case the reaction with

cancer antigens must be considered as a growth reaction. These workers refrain from speaking of a clinical-diagnostic reaction. Although the latter is the ultimate object of their investigation, they feel that the clinical application of their reaction to the diagnosis of cancer and pregnancy will not be possible for some time.

*Syphilis Immunity and Syphilitic Superinfection without Symptoms in the Human Individual*. By R. PRIGZE and E. VON RUTKOWSKI (Dtsch. med. Wochenschr., 1929, p. 1509).

These workers succeeded in producing a superinfection in a case of paresis, by inoculating spirochete material from the testicular syphilitic lesion of a rabbit. This superinfection ran a course without symptoms—a chancre immunity, the superinfection was proved to exist by the successful inoculation of extirpated inguinal nodes into a mouse and thence into a rabbit. Such a symptomless superinfection in syphilitic men had already been demonstrated by Kolle and his colleagues in experimentally infected rabbits. Such experiments would seem to indicate that the immunity of the syphilitic individual, even as in animals, is only an apparent immunity, a chancre immunity, which is not able to prevent the entrance of spirochetes into the organism. While these results throw new light upon the nature of the supposed "reinfection" of syphilis in a "cured case," the possibility that the spirochetes are latent in the case of paresis and grow when transferred to the new soil in the rabbit must be borne in mind. The theory of a superinfection cannot be regarded as proved beyond doubt.

*Action of Novasurol on Trichina Infection*.

By H. CHUKRI (Klin. Wochenschr., February 15, 1930, p. 298).

Jochweds and Pekielis in 1927 reported two human cases of trichinosis treated with novasurol with apparent great success. After the second injection of 12 ccm intravenously the temperature fell, the facial swelling greatly decreased, the muscle pains almost wholly vanished, and the stools became normal. After a week one case appeared perfectly well except for a slightly

subfebrile temperature and an eosinophilia of 30-40 per cent. The second case had a recurrence of symptoms on the 8th day after the first injection, but all symptoms disappeared within a few hours after the second injection and did not return. The authors asked the question as to the mechanism of the trichinocidal action of the novasurol. Since previously no drug has been known which will kill trichinae in the tissues or influence the course of trichinosis, it was deemed desirable to check up the observation made by Jochweds and Pekielis with experimental work. Chukri has therefore carried out experimental observations of the effect of novasurol upon rats infected with trichinae, with the following conclusions. Novasurol exerted no harmful or lethal action on intestinal, blood or muscle trichinae in the rat infected with such. No essential influence upon the course of rat trichinosis could be determined as the result of novasurol injections.

*The Race and Sex Distribution of the Lesions of Syphilis in 10,000 Cases*. By THOMAS B. TURNER (Bull. of Johns Hopkins Hospital, February, 1930, p. 159).

This paper is not concerned with the race and sex incidence in the general population, but with the incidence of the various manifestations of syphilis in a known syphilitic population. The statistics are based on the sex and race distribution of the lesions of syphilis among 11,818 consecutive admissions to the Syphilis Clinic of the Johns Hopkins Hospital above the age of 12 years. Of these patients 10,000 were syphilitics studied in sufficient detail to permit an accurate diagnosis, 996 were non-syphilitic and in 822 the diagnostic study was incomplete. The summary of this study is as follows. The total number of cases was approximately equally divided among the three stages of syphilis—early, tertiary and latent. Of the total cases 34 per cent had congenital syphilis. During the past 10 years there has been observed a steady decline in the number of cases of early syphilis in whites, especially white males. Genital chancres were observed but rarely in females. A slightly higher percentage of white males came under observation during the primary

stage than did colored males, and a much higher percentage of the former were seen in the sero-negative stage. Reinfection was observed more than 7 times as frequently in males as in females. Acute iritis occurred in 5.5 per cent of patients with secondary syphilis, although it was twice as frequent in negroes as in whites. The incidence of acute meningitis in whites was approximately twice that in negroes, and in males twice that in females. The incidence of neuro-occurrence was higher in whites than in negroes and higher in males than in females. In the late cases lesions of the skin and mucous membranes occurred with about equal frequency in the two races and the two sexes. The incidence in the late cases was 88 per cent. Lesions of the skeletal system were observed in 88 per cent of the total late cases. The incidence for whites was 57 per cent and for colored 94 per cent, while the incidence in each race was higher in the males. Syphilitic stricture of the rectum was confined almost wholly to colored females. Gumma of the lymph nodes was an uncommon manifestation. It occurred preponderantly in negroes. Clinically recognizable syphilitic affections of the cardiovascular system, excluding cerebral vascular lesions, occurred in 10 per cent of all late cases, the proportion of males to females and negroes to whites was approximately as 2 to 1. Uncomplicated aortitis, with or without aneurysm, occurred much more frequently in males than in females, and in negroes

than in whites. Aortic regurgitation was more than twice as common in males as in females, although it was nearly as common in whites as in negroes. Syphilitic angina pectoris was rare, but was more common in whites and in males, respectively, than in negroes and females. Central nervous system syphilis was observed in late syphilis in 39.3 per cent of white males, in 22.3 per cent of white females, in 15.9 per cent of colored males, and in 7.0 per cent of colored females. When serious disabling types of central nervous system syphilis only are included, the percentages are for white males 27.6, for white females 12.0, for colored males 5.9, and for colored females 2.2. General paresis was 7 times as frequent in whites as in negroes, and 28 times as frequent in white males as in colored females. Tabes dorsalis with or without optic atrophy or Charcot joint was much more common in white males than in white females or negroes of either sex. It was exceedingly rare in negro females. Cerebral vascular syphilis was observed somewhat more frequently in negroes than in whites. Of the syphilitics observed in the period of latency the proportion of females to males was as 3 to 2. The incidence of pulmonary tuberculosis in the negro syphilitics was decidedly less than the incidence in the general negro population. The incidence of pulmonary tuberculosis among the general dispensary class was not available. Diabetes mellitus was no more frequent among syphilitics than among non-syphilitics.



## Reviews

*The Bellevue Hospital Nomenclature of Diseases and Conditions* Department of Hospitals, City of New York Revised by the Committee on Clinical Records Approved by Dr William Schroeder, Jr, Commissioner 232 pages Paul B Hoeber, Inc, New York, 1929 Price in cloth, \$3 00

The first edition of the Bellevue Nomenclature was published in 1903, the third edition in 1911. The latter, to which some additions were made in 1922, has been in use since that date in the City Hospitals of New York City, as well as in many hospitals throughout the United States and Canada. In 1928 the committee appointed to revise the Nomenclature was instructed to make additions of new diagnoses rather than to reclassify and alter the old ones. Nevertheless, some change in the classification of disease had to be made to conform with the advances in medical knowledge. A few new subdivisions have been added, as Diseases of Allergy, of Metabolism and of Deficiency. The most radical change has been made in the cardiac section. Two subsections have been added, providing for etiological and physiological diagnoses. It is the intention to revise the Nomenclature once every five years. A captious critic might point out many deficiencies in this Nomenclature. Coccidioidal granuloma is not mentioned. Agranulocytosis is classed among the infectious diseases, in the index syphilis of the heart is not mentioned, but syphilis of the thyroid and thymus are, a strange evaluation of relative frequency and importance, Hodgkin's is put in the Miscellaneous Diseases, the term lymphoblastoma does not appear, the term acrodynia is preferred to Swift's disease, or Swift-Feer, etc. The classifications used savor too much of desk-research, rather than of a practical knowledge of modern nosology and pathology.

*Clinical Atlas of Blood Diseases* By A PINLEY, M D, M R C P, Research Pathologist, Cancer Hospital, London, Consulting Pathologist, Chelmsford Hospital, and STANLEY WYARD, M D, M R C P, Physician, Bollingbroke Hospital and Assistant Physician, Cancer Hospital, London 99 pages, 3 illustrations, 32 in color P Blakiston's Sons and Co, Inc, Philadelphia, 1930 Price in cloth, \$4 00 net

The publication of yet another book on clinical hematology might seem to require some justification, but the present one is intended to fill a need for which no other recent book even pretends to cater. The numerous atlases published at various times all have grave defects from the standpoint of the busy practitioner and the student. Many of them, such as Pappenheim's, contain so many illustrations that it is difficult for the non-specialist to make any practical use of them. More recent atlases give much space to the illustration of blood-pictures, but very little explanatory material. The present authors have tried to combine in one small volume the essential features of a textbook of hematology with an atlas, so that the practitioner will be able to find an account, albeit brief, of any hematologic malady with which he comes in contact, or conversely when presented with a blood-film, will be able to find an illustration corresponding with, at least, its general characters. The pictures have been all prepared from films stained by the Jenner-Giemsa method, except where noted. In all cases the magnification is 1,000 except for Plate 26, which is only 500. This is an interesting and valuable little atlas, the blood pictures are much better than the accompanying text. The pathology of the various conditions given is particularly poor. For instance, the statement is made the "Hodgkin's disease is no longer regarded as neoplastic," in spite of the increasing evidence

to that effect. Further, the authors seem to have little knowledge of the recent literature on the genetic neoplastic relationships of the leukemic and aleukemic lymphoblastomas, Hodgkin's, and mycosis fungoides. Ayerza's disease is not mentioned but a mistaken translation of "Cardiacos negros" is. The genetic relationships between Gaucher's disease, Niemann-Pick disease and generalized xanthomatosis is not hinted at, and there are many more omissions and deficiencies in the text, that may be explained by the great variation of opinion as to the nature of the condition described, and the difficulties attending the assemblage of these differences of opinion in so restricted a space. We believe, however, that the pictures are the best part of this book, and that they will be of great help to the medical student and to the worker in hematology.

*Diseases Transmitted from Animals to Man*

By THOMAS G. HULL, Chief Bacteriologist, Illinois Department of Public Health, Assistant Professor of Pathology and Bacteriology, University of Illinois, College of Medicine. With an Introduction by Veranus A. Moore, Director, New York State Veterinary College, Cornell University. 352 pages, 29 illustrations, 43 tables. Charles C. Thomas, Springfield, Illinois, 1930. Price in cloth, \$5.50.

Diseases which may be transmitted from animals to man immediately concern several groups of workers: the veterinarian, the physician, the laboratory worker and the health authorities. Each of these is engaged with a different phase of the problem, however, and views the subject from a different angle. Each has a different problem and approaches the subject from his individual standpoint. In this book, an attempt has been made to present each disease against a brief historical background, emphasizing its epidemiology and means by which infection may be prevented. Sufficient bacteriology is presented to balance the other material. There has been no special effort to present the special pathology, clinical symptoms or treatment, either in man or animals, although these subjects have not been wholly neglected. The material in this book is very

complete and valuable, and is well presented. It is thoroughly up to date, such recent subjects as Psittacosis, Tularemia and Undulant Fever being discussed fully as far as our knowledge of them goes. This book should be added to every internist's library, inasmuch as it contains so much valuable material bearing upon the occurrence of animal infections in man, information which should be added to the practical knowledge of all practitioners.

*The Bacteriophage and Its Clinical Applications*

By F. D'HERELLE, Professor of Bacteriology, Yale University School of Medicine. Translated by George H. Smith, Professor of Immunology, Yale University School of Medicine. 254 pages, numerous tables and charts. Charles C. Thomas, Springfield, Illinois, 1930. Price in cloth, \$4.00.

Each of the chapters of this text corresponds to one of the Lane Lectures, delivered at the Leland Stanford University, in October of 1928. In these lectures an effort was made to explain as fully as possible the extremely complicated subject of bacteriophage, and to make the text understandable to all intelligent persons, although addressed especially to practitioners of medicine. The therapeutic applications derived from these phenomena are considered, and it is claimed that these applications are daily being extended to embrace more and more diseases, and that today in most of the large hospitals of the world they form a recognized form of treatment. In this little volume D'Herelle expresses his concept of the nature of life. The six lectures are concerned with Bacteriophage, Bacterial Mutations, Nature of Bacteriophage, Infectious Diseases, Recovery and Immunity and the Use of Bacteriophage. The theories advanced in the Conclusions of this little book are so revolutionary that one of necessity hesitates as to their evaluation. If he is correct the cellular theory of life is shaken to its foundations and must be replaced by the theory of elementary micellae, which D'Herelle names "Protules." Such revolutionary and iconoclastic theories cannot be swallowed off-hand. Much more evidence

than D'Herelle assembles is necessary for their establishment

*Practical Psychology and Psychiatry* By B B BURR, M D Sixth Revised and Enlarged Edition, 378 pages, with 12 illustrations F A Davis Company, Philadelphia, 1930 Price in cloth, \$3 50

This manual is intended for use in training-schools for attendants and nurses and in medical classes, and as a ready reference for the practitioner The first edition appeared in 1898 The psychology section has been rather radically revised, certain new methods in treatment have received attention, and the chapter on the prevention of insanity has been enlarged and improved A brief chapter on aberrations in the sexual sphere has been added, as have also records of recent work in connection with paralytic dementia The book is divided into five parts Part I, Psychology, the Science of Mind, Part II, Symbolism in Sanity and Insanity, Part III, Insanity, Part IV, Management of Cases of Insanity, and Part V, the Prevention of Insanity The treatment of these various subjects is necessarily brief, but commendable for its sanity and good sense The main symptoms of the common forms of insanity are given, and a general outline of the treatment is added The chapters on the prevention of insanity and on Mental Hygiene are very good Still better is the sane attitude of the author toward crimes of the Loeb and Leopold and Hickman type, and the danger of sentimental extenuation of such crimes and of leniency toward such criminals

*Getting Well and Staying Well* A Book for Tuberculous Patients, Public Health Nurses and Doctors By JOHN PORRS, M D Introduction by J B McKnight, M D, Superintendent and Medical Director, Texas State Tuberculosis Sanatorium Second Edition, 221 pages The C V Mosby Co, St Louis, 1930 Price in cloth, \$2 00

Tuberculosis work is a teaching business Nearly everything that physicians learn of this disease, its prevention, cause and cure, must be translated into language for laymen's use In all cases of tuberculosis there

is a divided responsibility This book is written in the hope that it will aid patients, nurses and physicians in learning where their personal responsibility begins and where it ends It is also written to furnish answers to many of the numberless questions that come into the minds of patients, their families and family physicians The book is not the story of any one patient's personal experiences, but of many patients, many families, and many physicians, the rich and the poor, the educated and the uneducated For the purpose of emphasis many thoughts are repeated again and again This is a very practical and valuable book to be placed in the hands of the tuberculous patient Patients, physicians and nurses will obtain much benefit from its perusal It presents the details of the patient's daily routine in a simple and thoroughly practical manner The dangers and pitfalls that beset the case of tuberculosis are described in simple but effective language The book is filled with good sound sense, acquired from a wide experience in dealing with tuberculous patients The chapters on "Suspecting Tuberculosis" and on "Diagnosis" are especially well-written, and should be read by every physician entering the field of active practice

*Symptoms of Visceral Disease* A Study of The Vegetative Nervous System in Its Relationship to Clinical Medicine By FRANCIS MARION POTTENGER, A M, M D, L L D, F A C P, Medical Director, Pottinger Sanatorium for Diseases of the Lungs and Throat, Monrovia, California Fourth Edition 426 pages, 87 text illustrations and 10 color plates The C V Mosby Co, St Louis, 1930 Price in cloth, \$7 50

The fact that this book has reached its fourth edition in so short a time shows the interest created by this contribution to the newer physiologic medicine In this, the fourth edition, the author has attempted to discuss the principles involved in the study of visceral neurology, and to correlate them in such a manner as to make them readily applicable to clinical problems He emphasizes throughout the discussion the important

fact that action in a given case depends primarily upon the constitutional background of the patient, and secondarily upon the changes that are produced in that inherited structure by the environment. The influence of emotions upon the nerves and endocrines is stressed in such a manner as to emphasize the fact that abnormal physiologic action can result as much from psychical as from physical stimuli. The fact that the chief function of the vegetative nervous system is that of correlating and integrating action whereby activity in each organ and structure is brought into harmony with other organs and structures in states of health and into disharmony in conditions of disease receives greater emphasis in this than in the previous editions. Extensive additions have been made to many chapters, and a new chapter on Pharmacologic and Clinical Tests for Sympathicotonia and Parasympathicotonia has been added. The section on the lungs has been made particularly complete, and contains a classification of reflexes according to the afferent and efferent components which are responsible for the reflex. This same grouping of reflexes can be worked out for other important organs, and this is the task which the author has set for himself for the future. After an introductory chapter in which modern conceptions of disease are discussed, the material of the book is divided into three parts: Part I, The Vegetative Nervous System, treating of its anatomy and physiology; Part II, The Relationship Between the Vegetative Nervous System and the Symptoms of Visceral Disease; and Part III, The Innervation of Important Viscera with a Clinical Study of the More Important Viscerogenic Reflexes. In this book Dr Pottenger has assembled much important material not to be found together elsewhere. It is a valuable contribution to diagnostic medicine. The book is well printed, and the illustrations excellent. It is a work necessary to the up-to-date physician of today, and is warmly recommended.

*Lister Centenary Celebration* American College of Surgeons, Detroit, Michigan,

October, 1927 Descriptive Catalogue Presented by the Wellcome Historical Medical Museum, London

This beautiful catalogue was prepared for the Official Exhibition at the Lister Centenary Celebration held under the auspices of the American College of Surgeons at Detroit, Michigan, 1927, in connection with the centenary of the birth of Sir Joseph Lister. The Founder and Director of the Wellcome Historical Medical Museum, London, acquired the materials and was responsible for the official Lister Centenary Exhibition in the land of Listers' birth. The great interest and importance of that Exhibition was recognized at the Official Centenary Celebration held in London during April, 1927. Mr Wellcome felt that a collection of objects illustrative of Lord Lister's life-work would be of interest to members of the Medical and Surgical Professions in America. He, therefore, prepared and presented, through his Museum, this collection of replicas, including pictures, models, etc., to the American College of Surgeons for their exhibition at the Lister Celebration in Detroit. It is his desire that this collection shall form a permanent Exhibit in the Museum of the American College of Surgeons. The Catalogue of Exhibits consists of photographs illustrating Lister's life, work and honors, arranged chronologically, antiseptics, dressings and other materials as used by Lister in surgical operations, reproductions of various experiments performed by Lister, copies of diplomas and certificates, illustration of Lister's apparatus, instruments, etc. All of these are elucidated by extracts from Lister's writings, by an account of the evolution of Lister's system of antiseptic surgery by Sir Hector C Cameron, a life of Lord Lister, an account of pioneer work in antiseptic surgery, a review of various experimental researches by Lister, with sections on the influence of Lister's work and Lister's honours. The remainder of the catalogue is occupied with an account of the ceremonies attending the opening of the Wellcome Historical Museum, June 24, 1913. The volume is beautifully printed and is a valuable memento of the occasion.

## College News Notes

Dr Sam E Thompson (Fellow), Kerrville, Texas, has been elected Governor of the 47th District of Rotary International, representing practically all of the southern part of Texas

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The American Commission of the International Hygiene Congresses has formally invited the American College of Physicians and its members to be represented at the world health sessions to be held in Dresden, May 15—September 30, 1930. It is said that over two hundred scientific organizations will have their annual conventions converge in Dresden during this period, and will meet with the delegates of the League of Nations and twenty foreign governments whose participation in the Dresden meeting has been specified by legislative enactment. Complete details of the Congresses may be obtained by addressing Dr R Woerner, 393 Seventh Avenue, New York, N Y

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Dr George E Holtzapple (Fellow) and Dr Julius H Comroe (Fellow), both of York, Pa, have been promoted to the post of Advisor and Consultant to their respective groups of Visiting Physicians of the York Hospital

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The following Fellows of the College were on the program at the February meeting of the Homeopathic Medical Society of the County of Philadelphia

Dr G Harlan Wells, Philadelphia, "Insulin Treatment, its Action, Indications, Dosage, Technique"

Dr Donald R Ferguson, Philadelphia, "Common Metabolic Accidents to the Diabetic with Treatment"

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Dr Linn J Boyd (Fellow), New York, N Y, is the author of an article, "The Arudt-Schulz Phenomenon and Homeotherapy", which appeared in the February

number of the Journal of the American Institute of Homeopathy. The paper was read before the Bureau of Drug Pathogenesis, 58th Annual Convention of the American Institute of Homeopathy, Montreal, Canada, June, 1929

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Dr Joseph McFarland (Fellow), Philadelphia, Professor of Pathology, University of Pennsylvania School of Medicine, delivered the address at the Pasteur Assembly held at the Philadelphia College of Pharmacy on January 8

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Dr L Winfield Kohn (Fellow), New York City, was elected President of the Baltimore Medical Club for 1930-31 on February 13, 1930, at the meeting of the Club at the Commodore Hotel, New York. The guests of honor were Dr Alexius McGlannan, Professor of Surgery, University of Maryland, and Dr Harvey B Stone, Associate in Surgery, Johns Hopkins University Medical School

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Dr Harold Swanberg (Fellow), Quincy, Ill, is the author of an article entitled "Roentgen Pelvimetry (Thoms Method) and its Significance in Obstetrics" appearing in the March Issue of the Quincy Medical Bulletin

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Dr Dean B Cole (Fellow), Richmond, Va, is the President of the Virginia Tuberculosis Association. Their annual meeting was held at Roanoke, Virginia, on February 28. Dr H Kennon Dunham (Fellow), Cincinnati, was the chief speaker at the evening session

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The Southwestern Virginia Medical Society held its semi-annual meeting at Radford (Virginia) on March 24-25, and was addressed by Dr W S Leathers (Fellow), Dean of the School of Medicine, Vanderbilt

University, Nashville, Tenn, on the subject, "Preventive Medicine"

The Medical Society of Virginia will hold its annual meeting for 1930 at Norfolk on October 21, 22, and 23 Dr William S Thayer (Fellow), Baltimore, Maryland, will be one of the specially invited guests

Dr Walter Freeman (Fellow), Washington, D C, was one of the guest speakers of the Philadelphia College of Physicians, Section on Medical History, on March 10, 1930 Dr Freeman's subject was "Lewis Morgan The Note Book of a Tory Medical Student"

Dr Alf Hoff (Fellow), has been elected Chief of Staff of the Ancker Hospital, of St Paul, Minn

Dr Virgil E Simpson (Fellow), Louisville, Ky, delivered an address by invitation at the annual meeting of the Fayette County Medical Society, March 9, 1930, on the subject "Mendelian Law in Medicine"

Among new Regents of the American College of Physicians, elected during the Minneapolis Clinical Session, is Dr Walter L Bierring (Fellow), of Des Moines, Iowa, who is the President of the National Board of Medical Examiners

Among members of the Executive Committee of the National Board of Medical Examiners are the following Fellows of the College

Dr Lewis A Conner, New York, N Y  
Surgeon General H S Cumming of the U S Public Health Service

Surgeon General M W Ireland of the U S Army

Dr Waller S Leathers, Nashville, Tenn

Dr David Riesman (Fellow), Philadelphia, was recently elected President of the Medical Board of the Philadelphia General Hospital Dr Riesman succeeds Dr Herman Bryden Allyn (Fellow), Philadelphia, who had been President of the Medical Board for the past twenty-two years, and who recently resigned

Dr Daniel J McCarthy (Fellow), Philadelphia, will have charge of the neurologic Foundation at Temple University

Dr David A Tucker, Jr (Fellow), Cincinnati, is author of an article, "Medical Education", which appeared in the February Number of Clinical Medicine and Surgery

Dr William Devitt (Fellow), of Devitt's Camp, Allenwood, Pa, was the speaker at the "Health Talk" under the auspices of the Philadelphia County Medical Society on February 25 His subject was "Diet and Dissipation and Tuberculosis"

Dr Carl V Vischer (Fellow), Philadelphia, is author of the contributed article for December in the Hahnemannian Monthly, "Acute Military Tuberculosis Report of Cases with Recovery"

Major L R Poust (Fellow), formerly stationed at the Station Hospital, Fort Sam Houston, Texas, as Chief of the Tuberculosis Section, was recently transferred to Manila, P I, where he is serving as Chief of the Medical Service in Sternberg General Hospital

Acknowledgment is made of the receipt of the following publications contributed by the authors to the Library of the American College of Physicians

Dr William H Riley (Fellow), Battle Creek, Mich

"The Reactions of the Body to the Short Cold Bath"

"A Clinical Study of 264 Cases of Pernicious Anemia with Special Reference to the Involvement of the Central Nervous System"

Dr George L Waldbott (Associate), Detroit, Mich

"Allergy as Cause of Epileptiform Convulsions"

Dr B S Pollak (Fellow), Secaucus, N J

"Tuberculin as a Diagnostic and Therapeutic Agent in Tuberculosis"

"Some Points in the Early Diagnosis of Clinical Tuberculosis"

"Oration in Medicine"

"The Relation of Tuberculosis to Other Communicable and Preventable Diseases"

"Pulmonary Hemorrhage, Its Etiology, Pathology and Therapy"

"Tuberculosis in Infancy and Childhood"

"The Heritage of Sanitation"

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Dr George E Pfahler (Fellow), Philadelphia, is the author of an article, "Shall Cancer of the Uterus be treated by Surgery or Radiation?", which appeared in the February number of the Pennsylvania Medical Journal

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Dr G Harlan Wells (Fellow), Philadelphia, was recently appointed an Associate Editor of the Journal of the American Institute of Homeopathy

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Dr Linn J Boyd (Fellow), New York, is author of an article "Neglected Aspects of Symptomatology," which appeared in the January Number of the Journal of the American Institute of Homeopathy

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Dr G Morris Golden (Fellow), Philadelphia, is author of an article, "Silent Gap in Blood Pressure Its Clinical Significance," which appeared in the December Issue of the Hahnemannian Monthly

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Major L R Poust (Fellow), Chief of the Medical Service, Sternberg General Hospital, Manila, P I, has tendered his services to the Philippine Anti-Tuberculosis Society, and is now instructing a group of Filipino doctors at Santol Hospital for the tuberculous, the indications for, and the institution of collapse therapy, in the treatment of pulmonary tuberculosis

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During the Annual Congress on Medical Education, Medical Licensure and Hospitals, held in Chicago, February 17-19, 1930, the following Fellows of the College delivered stated addresses

Dr William Gerry Morgan, President-Elect of the American Medical Association, Washington, D C

Dr Ernest E Irons, Clinical Professor of Medicine and Dean, Rush Medical College, Chicago, Ill

Dr Torald Sollman, Professor of Pharmacology and Materia Medica and Dean, Western Reserve University School of Medicine, Cleveland, Ohio

Dr W McKim Marriott Professor of Pediatrics and Dean, Washington University School of Medicine, St Louis, Mo

Dr L G Rowntree, Professor of Medicine, Mayo Foundation for Medical Research, Rochester, Minn

Dr D J Davis, Dean, University of Illinois College of Medicine, Chicago, Ill

Dr Howard T Karsner, Professor of Pathology, Western Reserve University School of Medicine, Cleveland, Ohio

Dr Charles C Bass, Professor of Experimental Medicine and Dean, Tulane University School of Medicine, New Orleans, La

Dr Kenneth M Lynch, Professor of Pathology, Medical College of the State of South Carolina, Charleston, S C

Dr Waller S Leathers, Dean, Vanderbilt University Medical School, Nashville, Tenn

Dr James B Herrick, Professor of Medicine, Rush Medical College, Chicago, Ill

Dr Peter Murray, New York, N Y

Dr Merritte W Ireland, Surgeon-General, United States Army, and Member of the Council on Medical Education and Hospitals of the American Medical Association, Washington, D C

Dr Walter L Bierring, Secretary, Federation of State Medical Boards, Des Moines, Iowa

Dr David P Barr, Busch Professor of Medicine, Washington University School of Medicine, St Louis, Mo

Dr Arthur D Dunn, Professor of Clinical Research, University of Nebraska College of Medicine, Omaha, Nebr

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Dr Edwin Henes, Jr (Fellow), reports that the published proceedings of the Detroit Assembly of the Interstate Postgraduate Medical Association, of which he is Editor, will appear early in April. The volume will be dedicated to Thomas A

Edison, and will contain the entire Detroit Program, to which many Fellows of the College contributed

Dr W Samuel Kerlin (Fellow), Shreveport, Louisiana, was recently elected First Vice President of the Shreveport Medical Society

Dr Warren T Vaughan (Fellow), Richmond, Virginia, was recently elected Second Vice President of the Richmond Academy of Medicine

Dr W Bernard Kinlaw (Fellow), Rocky Mount, North Carolina, has been elected a Vice President of the Seaboard Medical Association of Virginia and North Carolina

Dr Beverley R Tucker (Fellow), Richmond, Virginia, recently published a one-act play, "The Lost Lenore", dealing with the life of Edgar Allan Poe

Dr Otto T Brosius (Fellow), has recently transferred from Superintendent, Medical Department, Chiriqui Land Co, Puerto Armuelles, R of P, to Superintendent, Medical Department, United Fruit Co, Almirante, Bocas del Toro, R of P

Dr Albert F R Andresen (Fellow), Brooklyn, has been Clinical Professor of Medicine (Gastroenterology) of Long Island College Hospital (Medical School) for the past ten years. He has also been attending physician (Gastroenterologist) to the Long Island College Hospital and Chief of the Gastroenterological Clinic at Polhemus Memorial Clinic. He is at the present time President of the New York Gastroenterological Association, Secretary of the Section on Gastro-Enterology and Proctology of the American Medical Association, Chairman of the Committee in charge of the Friday Afternoon Practical Lectures of the Medical Society of the County of Kings. He has recently delivered the following addresses

"Medical Aspects of Gall-Bladder Disease", a lecture before the Medical Society of the County of Kings, December 6th, 1929

"Medical Aspects of Peptic Ulcer", before a joint meeting of the Brooklyn Society of Internal Medicine and the Brooklyn Surgical Society, February 6th, 1930

Dr Noxon Toomey (Life Fellow), St Louis, is the author of "The Treatment of Skin Diseases—in Detail". The work is Volume Three of Doctor Toomey's "Principles and Practice of Dermatology". The work was published by the Lister Medical Press, St Louis, on March 15, 1930. It contains 512 octavo pages and fully discusses the treatment of the rarer as well as the commoner skin diseases, some three hundred in number

Dr Clifford J Barborka (Fellow), Rochester, presented a paper on "The Results of the Use of the Ketogenic Diet in One Hundred Cases of Adult Epilepsy" before the Association for Research in Nervous and Mental Diseases at the Commodore Hotel, New York City, on December 28, 1929

Dr E L Sevringhaus (Fellow), Associate Professor of Medicine at the University of Wisconsin Medical School, has been pursuing postgraduate study at the Graduate School of Medicine of the University of Pennsylvania. He was a recent visitor at the College headquarters

Acknowledgment is made of the following gifts to the College Library of publications by members of the College

Dr Frank Smithies (Master), Chicago, Ill

1 Books  
"Cancer of the Stomach" (with Albert J Ochsner, M D)

Reprints  
"Tuberculous Enterocolitis" (With Weisman & Fremmel)

"Parasitosis of the Bile Passages and Gall Bladder"

"On the Present Status of the Treatment of Peptic Ulcer"

"Protozoiasis Occurring in Temperate Zone Residents"

"The Phenomena Concerned with 'Reactions' Following the Transfusion of Blood" (With Kordenat)



- "Biliousness"
- "Certain Factors to be Considered in Prognosing Cure of Peptic Ulcer"
- "Aseptic Irritative Phlebitis Following Intravenous Injection of Sodium Salt of Tetrabromphenolphthalein" (With Oleson)
- "Necessity for Caution in the Employment of High Voltage Roentgen-Rays as a Therapeutic Agent Against Malignant Diseases Acute Adrenal Insufficiency and Death as Sequelae"
- "The Visualization of the Biliary Tract A New Method by Intravenous Injections of Tetrabromphenolphthalein" (With Oleson)
- "Diagnosis and Clinical Manifestations of Cardiospasm Associated with Diffuse Dilatation of the Esophagus"
- "Late Cardiorespiratory Manifestations of 'Gassing' As Exhibited by Returned Soldiers"
- "Significance of Etiologic Factors in the Treatment of Peptic Ulcer"
- "Pericholecystitic Adhesions"
- "The Nonsurgical Management of Peptic Ulcer by the 'Physiologic Rest' Method"
- "Chronic Intestinal Stasis and Its Associated So-Called Toxaemia"
- "Blood-Cell Changes in Gastric Cancer"
- "Contributions of the Twentieth Century Toward a Better Understanding of Gastro-Intestinal Ailments"
- "Present-Day Treatment of Intestinal Protozoiasis and Factors that Determine Its Efficacy"
- "Anemia of the 'Hemolytic' or 'Pernicious' Type Consequent Upon Chronic Lead Poisoning, Arteriosclerosis, Myocardial Hypertrophy and Degeneration, Infections of Gums and About the Roots of the 'Teeth'"
- "Observations upon the Phenoltetrachlorophthalein Test for Liver Function" (Higgins)
- "Syphilis of the Colon and the Lower Bowel with Report of Three Cases" (Karshner)
- Dr Virgil E. Simpson (Fellow), Louisville, Ky
- Reprints
- "Tularemia"
- "Diseases of the Cardiovascular System Due to Acquired Syphilis"
- "A Discussion of the Probable Etiological Relationship Between Peptic Ulcer and Vagatonic Syndromes"
- Dr Frederic J Farnell (Fellow), Providence, R I
- Reprints
- "Industry and Social Welfare"
- "Welfare and Mental Hygiene"
- "The Unmarried Mother"
- Dr Philip B Matz (Fellow), Washington, D C
- Reprint
- "Improved Colorimetric Procedures for the Quantitative Estimation of the Proteins of the Cerebrospinal Fluid" (With Novick)
- Dr Joseph D Gray (Fellow), Augusta, Ga
- Reprint
- "Agranulocytosis"
- Dr Miles J Breuer (Fellow), Lincoln, Nebr
- Reprint
- "Mental Hygiene of Adolescence"
- Dr Walter M Simpson (Fellow), Dayton, Ohio
- Reprint
- "Recent Developments in Tularemia"
- 
- Dr Milton C Borman (Fellow), has left Montgomery, W Va, and is now located at the Sacred Heart Hospital, Milwaukee, Wisconsin
- 
- Dr Murray B Gordon (Fellow), Clinical Professor of Pediatrics, Long Island College Hospital, New York, addressed the Medical Society of the County of Nassau, Mineola, Long Island, on "Endocrine Diseases and Disorders in Children" on February 27, 1930, and the Health Forum of the United Israel Zion Hospital, Brooklyn, on "How to Prevent Contagious Diseases in Children" on March 5, 1930
- 
- Dr F Garm Norbury (Fellow), Associate Physician, Norbury Sanatorium, Jacksonville, Illinois, departed March 29th for Amsterdam, Holland
- Dr Norbury will do special work in the University of Amsterdam, Department of Neurology, under Prof B Brouwer, and Post-graduate course in Psychiatry, Maudsley Hospital, London

## COLLEGE MEMBERSHIP

At the Minneapolis Clinical Session, 201 Fellows were inducted to Fellowship and 67 Associates were elected. The total membership now numbers 2,360, of which 6 are Masters, 1800 are Fellows and 554 are Associates.

Among the Fellows and Masters, there are 19 Life Members who have subscribed to the Life Membership Fund. The complete list is printed below.

Lewellys F Barker	Baltimore, Md
Oscar Berghausen	Cincinnati, Ohio
Robert Bernhard	New Orleans, La
Carl R Comstock	Saratoga Springs, N Y
Ernest Falconer	San Francisco, Calif
J A Lepak	St Paul, Minn
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Francis Pottenger	Monrovia, Calif
Austen Fox Riggs	Stockbridge, Mass
John G Ryan	Denver, Colo
Adolph Sachs	Omaha, Nebr
William D Sansum	Santa Barbara, Calif
Frank Smithies	Chicago, Ill
Alfred Stengel	Philadelphia, Pa
Noxon Toomey	St Louis, Mo
M L Turner	Berwyn, Md
A H Waterman	Chicago, Ill
Bernard L Wyatt	Tucson, Ariz

## 1931 CLINICAL SESSION

March 23-28, 1931, has been set for the time of the Fifteenth Annual Clinical Session of the American College of Physicians at Baltimore, Maryland. By resolution of the Board of Regents, adopted at the last Clinical Session, the President of the College becomes responsible for the General Scientific Programs, during the afternoons and evenings. The local General Chairman is responsible for the general arrangements and for the programs of Clinics and Demonstrations at the various hospitals and institutions. Dr Sydney R Miller, President, therefore, is preparing the general program of scientific papers, and Dr Maurice C Pincoffs is arranging the program of clinics. Both of these officers will appreciate helpful suggestions and recommendations from members of the College.

## OMISSION

In the March Issue of ANNALS OF INTERNAL MEDICINE, in the list of new Officers of the American College of Physicians for 1930-31, the name of Dr John A Lichty, Clifton Springs, New York, was omitted as the Third Vice President.

## REGENTS' MEETING

A special meeting of the Board of Regents will be held at the College headquarters in Philadelphia on May 4, for the purpose of examining the credentials of new candidates for Fellowship, for determining the final details of the John Phillips Memorial Fund, for preliminary plans for the Fifteenth Annual Clinical Session at Baltimore in 1931 and to transact the regular business of the College.

Inasmuch as the regulations of the Board of Regents require that proposals for Fellowship be on file thirty days in advance of action, only those proposals received up to and including April 5 will be acted upon at this meeting.

The Board of Regents will probably hold their regular fall meeting during the month of November.

## NEW ADVERTISERS

Attention of readers and subscribers is drawn to the following new advertisers in this issue of ANNALS OF INTERNAL MEDICINE.

Page 3 Devitt's Camp, Allenwood, Pa

Page 14 The Wyatt Clinic, Tucson, Ariz

Page 17 Lister Medical Press, St Louis, Mo

The Columbus Rural Rest Home also has returned to our advertising columns, although they are not new.

Fellows of the College are in each case responsible for this support given to ANNALS OF INTERNAL MEDICINE, Dr William Devitt, F A C P, is the Physician-in-Charge of Devitt's Camp, Dr Bernard L Wyatt is the head of The Wyatt Clinic, and Dr Noxon Toomey, F A C P, is the author of the book, "Treatment of Skin Diseases in Detail", advertised by the Lister

**Medical Press** It is hoped that these advertisers, as well as every other one who has advertised in our journal in the past, will be well supported by Fellows and Associates of the College, and by our readers and subscribers everywhere

### PLACEMENT SERVICE

Announcement in the February Issue of **ANNALS OF INTERNAL MEDICINE** of the fact that the Executive Offices will act as a sort of clearing house through which members of the College may seek assistants or may obtain new connections, has resulted in some additional positions, as well as candidates, having been reported

The College will assist in securing authentic information, but cannot assume responsibility in connection with recommendations. The purpose of the Executive Offices is to serve the membership in the best possible ways. Inquiries should be sent to E. R. Loveland, Executive Secretary, 133-135 S 36th Street, Philadelphia, Pa

### VACANCIES

No 101—For a young man, graduated from a good school, and with good hospital training, who is particularly interested in clinical laboratory work and pathology, and who has also had some ground work in radiological work. Should be capable of heading up the entire laboratory department, including the clinical laboratory and the X-ray department. Preference for an unmarried Protestant. Location in the South

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No 4—An Associate of the College desires an assistantship or an association with some good clinic, willing to go anywhere, if there is a promising future, personal interview desirable, as well as period of probation to show ability, extensive training and experience in diseases of the heart and lungs and in insurance examinations, age 36, married, M.D., Tulane University, postgraduate work in Internal Medicine at New York, Chicago, Philadelphia and Mayo Clinic, special examiner during World War in diseases of heart and lungs, since engaged in civil practice, doing only Internal Medicine, with important teaching and hospital appointments

### NATIONAL HOSPITAL DAY

Hospitals throughout the United States and Canada are beginning plans for the tenth observance of National Hospital Day, May 12, according to information reaching Dr. J. R. Morrow, superintendent, Bergen Pines, Oradell, N. J., chairman of the National Hospital Day Committee of the American Hospital Association

While some institutions which have observed the day since its start are seeking new ideas, the majority of the hospitals will have "open house", reunion of babies, inspection of departments and other features which met with such success in previous years. Some of them undoubtedly have had the same experience as a hospital which decided to omit its "baby show" one year and found that the mothers, who had gathered in larger numbers than on the previous occasion, were greatly disappointed.

That more small hospitals will observe May 12 this year than in the past is the belief of some of the members of the National committee, owing to the tribute paid to small hospitals in rural sections by President Hoover in his endorsement of National Hospital Day.

Hospital councils in some cities focus all their attention at March and April meetings on plans for a joint observance of National Hospital Day. The Chicago Hospital Asso-

ciation is among those doing this at this time. This association, incidentally, already has been tendered time on two radio stations.

The national committee is in touch with large manufacturers and others using nation-wide radio hookups and hopes to extend the radio publicity given National Hospital Day last year. Many hospitals also are

making arrangements for individual radio programs, as in the past.

Most of the hospitals conducting schools of nursing which will have a National Hospital Day program will give considerable attention to a presentation of facts about nursing education and nursing service, keeping in mind that May 12 is the anniversary of the birth of Florence Nightingale.

## OBITUARY

Dr Florence Chadwick (Fellow), Detroit, Michigan, died on October 31, 1929. She was born at North Dighton, Mass., in 1879, and attended the Massachusetts Normal School and the Boston Normal School of Gymnastics. Later she determined to follow a medical career, and attended the Medical School of the University of Michigan, from which she graduated in 1912. After a year's internship in the New England Hospital of Boston, she went to Detroit, spending one year as interne and another year as resident physician in the Woman's Hospital.

She was a member of the Alpha Omega Alpha, Sigma Psi and Alpha Epsilon Iota Fraternities. She was a member of the Wayne County Medical Society, the Michigan State Medical Society, the American Medical Association, and had been a Fellow of the American College of Physicians since February 24, 1926.

She won the respect and admiration of her colleagues, both as a physician of great ability and as a woman of high ideals. To her patients, she was an indefatigable worker, constantly at their service as a friend or counselor both in sickness and in health. To the community she contributed generously of her time and skill through her many years of charitable work at Harper Hospital, Woman's Hospital and the Children's Aid Society. She was a powerful character, as a member of the Central Bureau of Nurses, in approving nursing conditions in Detroit. Her death was a grievous loss to her

colleagues, her clientele and the entire community.

---

Dr Samuel K. Pfaltzgraff (Associate), York, Pa., died November 22, 1929, following a sudden attack of coronary thrombosis. He was one of York's leading physicians, and at the time of his death was Dermatologist to the York Hospital and President of the general staff.

Dr Pfaltzgraff received his early training in the York County Academy, and was graduated from the University of Maryland in 1886. He later took several postgraduate courses in various medical schools, more especially in the domain of Dermatology. He was a member of his county and state medical societies, of the American Medical Association, and an Associate of the American College of Physicians.

Dr Pfaltzgraff served as coroner of York County, was a member of the City Board of Health, and also a member of the board of school control. He was also a very prominent figure in Democratic politics, being a delegate to the national conventions in Baltimore, St. Louis and San Francisco. He declined the office of postmaster, during the administration of President Wilson.

During the World War, Dr Pfaltzgraff was a member of the Medical Advisory Board, and was very active in all patriotic movements. He was a member of numerous civic and benevolent organizations. In his will, he directed that the sum of ten thousand

dollars be given to the Yoik Hospital for the establishment of a dermatological clinic. He is survived by his wife, Mrs Mary Pfaltzgraff.

(Supplied by Julius H. Comroe, M.D., F.A.C.P., Yoik, Pa.)

---

Dr James Irvin Johnson (Fellow) of Pittsburgh died suddenly on Sunday, February 9th, of coronary disease.

Dr Johnston was born in the year 1868, graduated from the University of Pennsylvania in 1893; Intern, Presbyterian Hospital, Philadelphia, 1893-95, Staff Physician, Presbyterian Hospital, Pittsburgh, 1895-1907, Physician Rosalia Foundling Asylum 1895-99. At the time of his death he was Senior Physician and Vice-President of Staff at Mercy Hospital, Pittsburgh, Assistant Professor of Medicine, University of Pittsburgh School of Medicine, Consulting Physician, Eye and Ear Hospital, Pittsburgh. He was a member of Phi

Alpha Sigma fraternity, ex-President, Pittsburgh Academy of Medicine (1917), President (1929), Allegheny County Medical Society, Chairman, Section of Medicine (1922), Pennsylvania State Medical Society, Fellow, American Medical Association, Member, American Therapeutic Society, Associate Fellow, Society for Biological Research, Fellow, American College of Physicians since 1917. He was author of a number of articles in medical journals and co-author of "Epidemic Influenza," a book published by the University Press, Pittsburgh.

Dr Johnston is survived by his widow, Mrs Bertha G. Johnston, two sons, S. Paul Johnston and Dr John M. Johnston, and an adopted son, Samuel E. Gill.

Dr Johnston's useful career was seldom interrupted by illness, and he continued his professional activities until a few hours of his death.

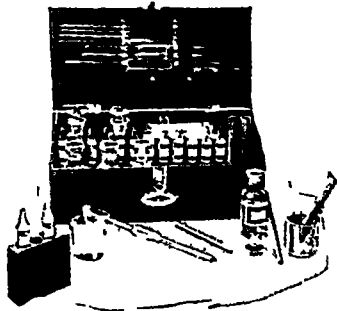
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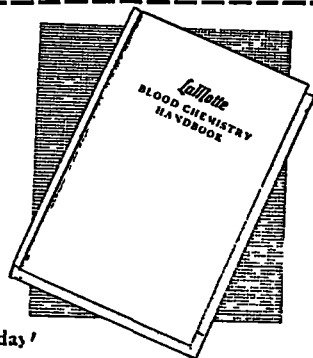
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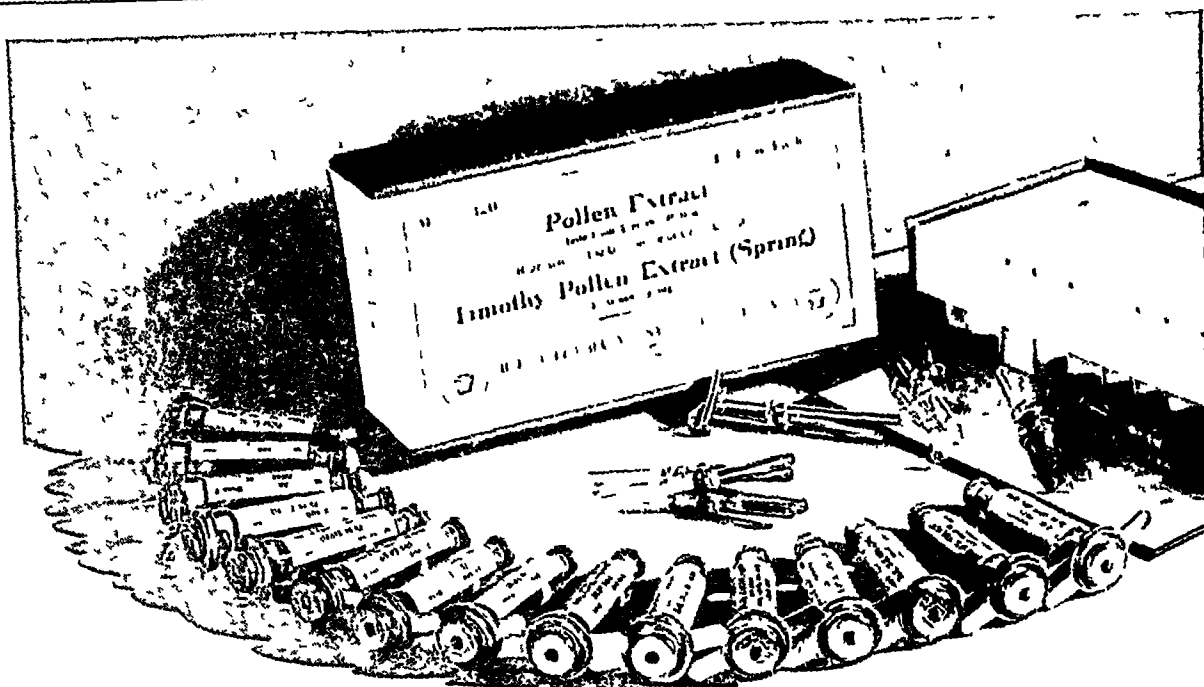
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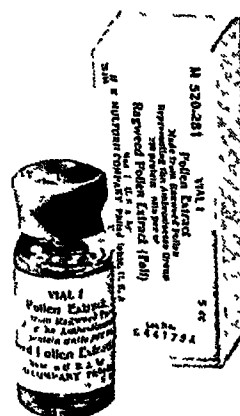
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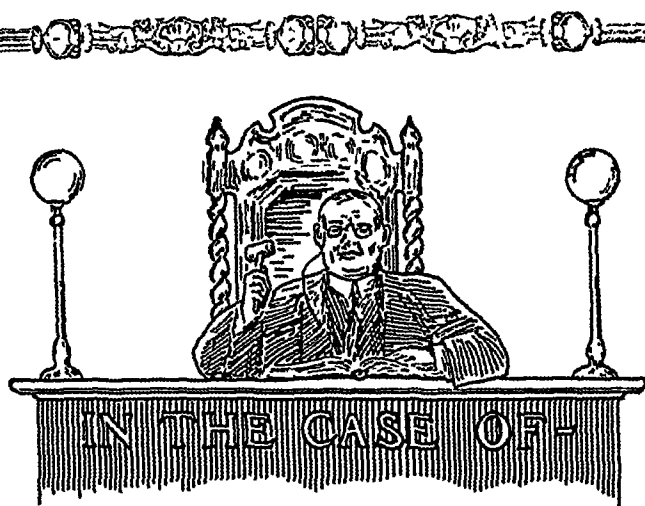
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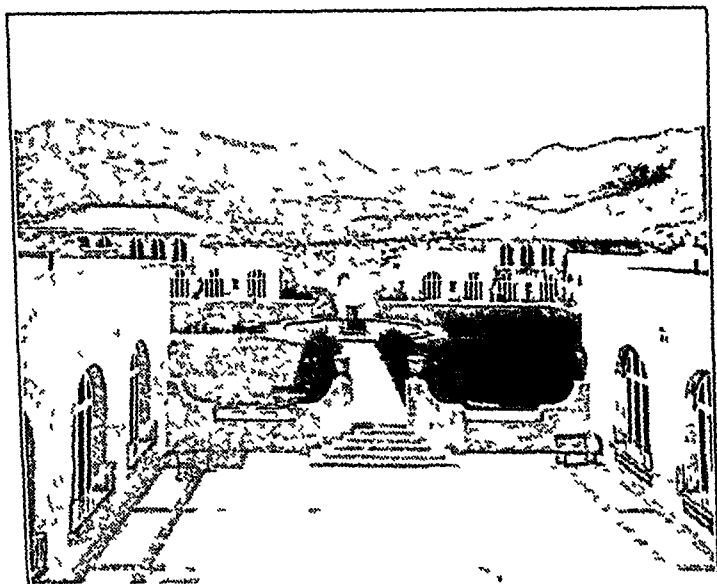
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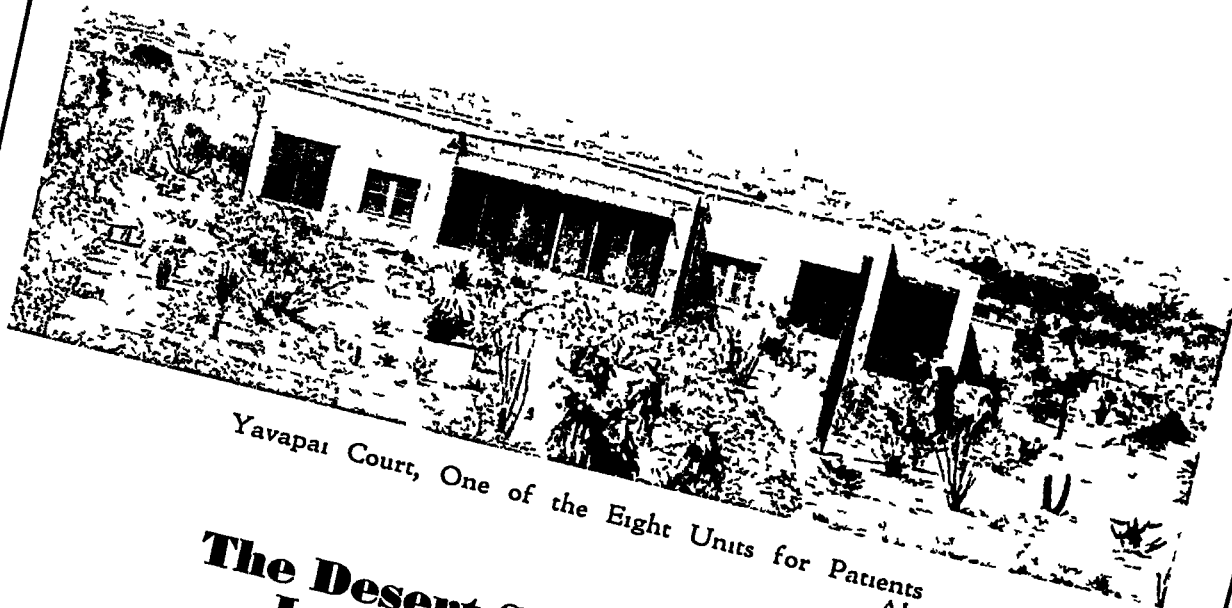
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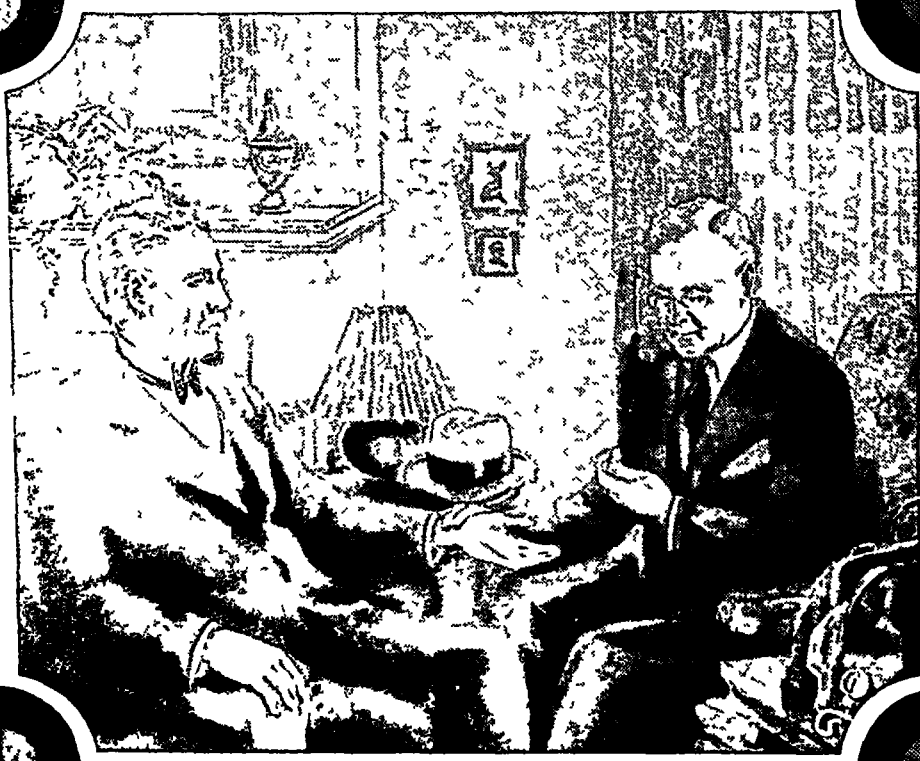
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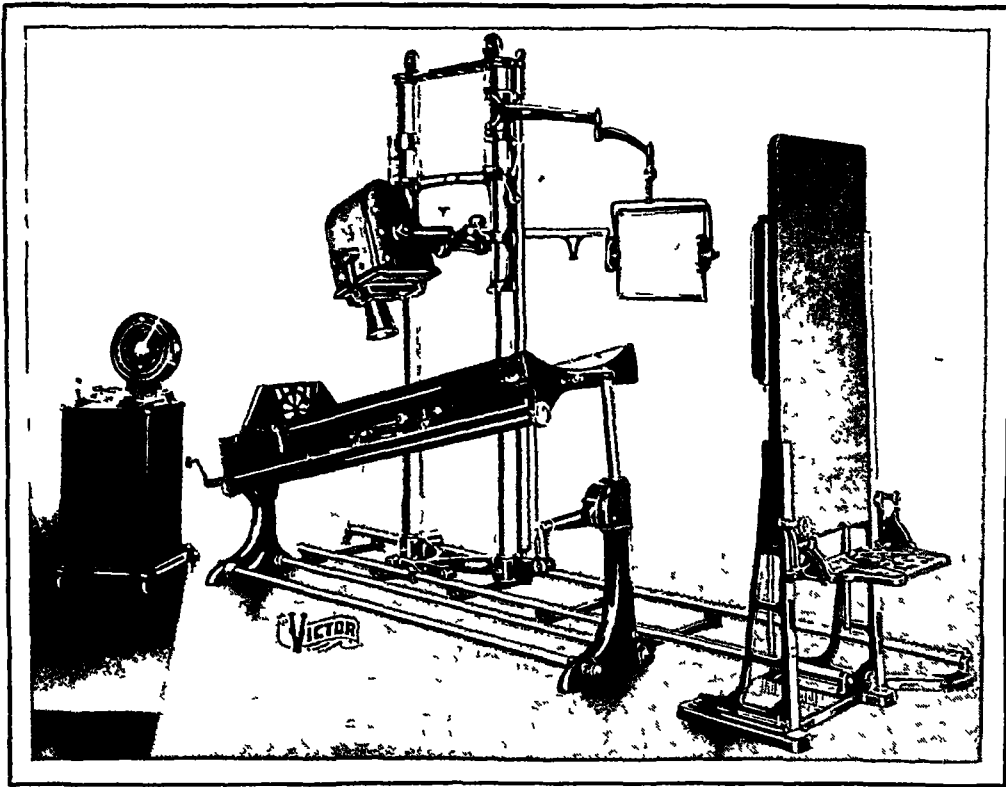
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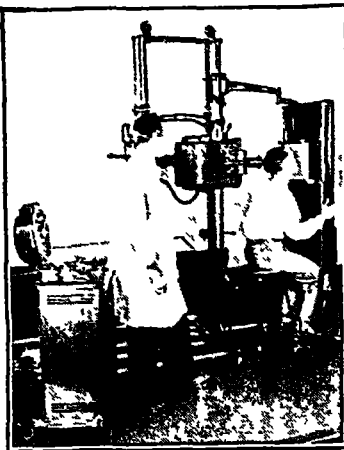
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# Venous Pressure and Vital Capacity

By EDGAR V ALLEN, M D,\* and MAX HOCHREIN, M D, *Medizinische Universitätsklinik, Leipzig, Germany*

**M**ETHODS for estimating the normal vital capacity without actual measurement have been varied. Shepard and Myers, and West and Dreyer compared vital capacity to size of body and succeeded in determining normal values. West believed that the value obtained by measurement of the surface of the body was the best for determining the normal vital capacity. Dreyer showed the relationship between the vital capacity, body weight and circumference of the thorax. Similar measurements were made by Rowe. Kharina compared age, weight, size, circumference of thorax, sitting height, and vital capacity, and found that the cube of the sitting height possessed a relationship to the vital capacity which could be expressed by the number 21. With the help of this calculation, he studied numerous cases in order to determine the influence of age, sex, and race. McCloy determined the vital capacity of 4,000 students and found that the deviation from normal was not in excess of 88 per cent. Nanagas and Santiago showed that the average value for the vital capacity is practically constant in different races. The relationship of volume of the thorax

and vital capacity was studied by Bilard and Gourdon. They found the following proportions of volume of thorax to vital capacity:

Volume of thorax	50	60	70	80	90	100	110	120	130
Vital capacity	09	10	14	15	19	20	23	265	265

Rabinowitch studied vital capacity and basal metabolism and found that when the vital capacity increased, the basal metabolism fell.

Wachholder used the vital capacity as a standard to determine the fitness of persons for athletic undertakings. The value was determined during rest and again after running from 150 to 200 meters. He found the following groups: (1) Good athletes, the vital capacity fell from 150 to 200 cc after the race and returned to the previous value in from two to three minutes. (2) Athletes with poor reserve, the vital capacity fell from 200 to 500 cc and returned to the original value in approximately three minutes. (3) In persons with labile circulatory systems and in constitutionally weak individuals, the vital capacity was reduced 500 cc or more and returned to the previous value only after five or more minutes.

The vital capacity has been determined in various diseases and occa-

\*Fellow of the National Research Council

sionally has been used as a diagnostic and prognostic aid. Okado found normal values in patients with beri-beri. Myers and Rice found diminished values in cases of pleuritic adhesions, pulmonary tuberculosis and after healing had taken place in empyema. In pneumonia, Dreyer and Burrell demonstrated increase of the vital capacity with improvement, and decrease with increasing severity. According to Arnett and Kornblum, the vital capacity falls off sharply from the second to the fourth day after the crisis of pneumonia, and, in cases with normal convalescence, reaches approximately 70 per cent of the normal value thirty-five days after the crisis. Relapse in the course of pneumonia manifests itself relatively early by diminution of the vital capacity. Leas determined the values during the breathing of moist and dry air and found that the vital capacity of patients with bronchial asthma and bronchitis increased 25 per cent during the breathing of dry air. Patients with bronchial spasm, pulmonary edema, and diminished pulmonary expansion due to congestion from cardiac disease disclosed no change in the vital capacity when the patient was breathing moist or dry air. Peabody investigated the vital capacity systematically in patients with circulatory disease, and, with Sturgis, found it to be diminished. This decrease was thought not to be due to weakness of the muscles of respiration, as he found normal values in very weak patients with pernicious anemia. He found continually normal values, during repeated determinations, under conditions which pre-

supposed tiring and weakness of the respiratory muscles. Peabody recommended the determination of vital capacity as a method for ascertaining the circulatory efficiency. He differentiated the following groups: patients with circulatory disease but with normal body performance and normal vital capacities, patients who are able to do light work and have vital capacities between 70 and 90 per cent of the normal, patients who are unable to work and have vital capacities between 50 and 70 per cent of the normal. Blumgart and Weiss studied various factors of the circulation, such as circulation time, arterial pressure, and venous pressure and brought these into relationship with the vital capacity. Frequently they found diminished vital capacity associated with slowing of the pulmonary circulation. Arnett and Kornblum studied vital capacity in cases of various kinds of valvular heart disease, and showed it to be less dependent on pathologic change than on the functional status of the heart. Engelhard believed that the carbon dioxide should be used in the determination of the vital capacity. Lundsgaard attempted to determine the cause of the diminution of the vital capacity in patients with cardiac disease. He found, in such patients, a change in the relationship of vital capacity, tidal air, residual air and complementary air. Diminution in the vital capacity could occur as a result of decrease of the total capacity as well as of increase in the amount of the residual air.

As determination of the vital capacity is very simple with a common

spirometer, we have made daily studies on a large number of patients with different diseases. We have found a regular diminution of the vital capacity in patients with circulatory insufficiency. The relationship is, however, not between anatomic cardiac changes and the vital capacity but between the functional status of the circulation and the vital capacity. We have demonstrated, also, a close relationship between the venous pressure and the vital capacity.

Patients with circulatory insufficiency and high venous pressure have definitely decreased values for vital capacity. If the condition of the patient is improved, then the venous pressure falls and the vital capacity increases (table 1). Both the vital capacity and the venous pressure were studied on the admission of a large number of patients to the hospital, and after eight days of intensive therapy. The results of the therapy are definitely recognizable. The increase of the venous pressure and the decrease of the vital capacity do not stand in linear relationship one with the other. Patients who come into the clinic in a badly decompensated state, and are successfully treated, seldom acquire more than 70 per cent of the expected normal vital capacity even after ten weeks of intensive treatment, and at a time when the venous pressure has long been at a normal level.

Sudden sinking of the venous pressure can be produced by the withdrawal of venous blood (table 2). The vital capacity shows no immediate great change but there is a definite tendency toward an increase, a fact in

keeping with the patients' statements that they breathe more easily. Venesection has no definite effect on the pulse rate and the arterial pressure.

Many of our patients had pulmonary as well as circulatory disease. If pulmonary disease alone were present, the venous pressure was normal whereas the vital capacity was diminished (table 3). If cardiac insufficiency occurred in the course of pulmonary disease, there was increased venous pressure as well as diminished vital capacity.

The close relationship between breathing and circulation, in mechanical and physiochemical respects, allows many speculations concerning the changed vital capacity in cases of circulatory insufficiency. Such a change cannot be due to increased carbon dioxide tension of the blood, for such an increase will not diminish the vital capacity if the circulatory efficiency is normal. Nervous (Breuer-Heringscher reflex) or mechanical influences must be considered to explain altered vital capacity in cases of circulatory disease. In addition to the explanations already offered by other authors, we have considered over-filling of the lungs with blood, thus producing a mechanical effect on the vital capacity. There is also loss of elasticity of the lung, which is followed by an increase of the residual air.

#### SUMMARY

The venous pressure is increased and the vital capacity decreased in patients with cardiac insufficiency due to any cause. Improvement of the circulatory status is attended by sinking of the venous pressure and increase

TABLE I  
CAPACITY AND VENOUS PRESSURE IN CASES OF CIRCULATORY  
FAILURE SHOWING THE EFFECT OF TREATMENT ON THE VITAL  
INSUFFICIENCY

On Admission to the Hospital				After Eight Days of Treatment			
Case	Diagnosis	Age	Clinical Symptoms	Pulse Rate	Resp Rate	Blood Pressure Arterial Venous	Vital Capacity
1	Myocardial degeneration, lung edema, auricular fibrillation	65	Cyanosis, dyspnea, marked edema, enlarged liver, bloody sputum	92	32	165/20 30 0	1 0
						80 20 20 0	190/140 1 2
							Diminished cyanosis and dyspnea, liver size and edema markedly diminished, no blood in sputum
2	Hypertension, cardiac asthma, Egg arborization block, T waves in leads 1 and 2 inverted	53	Attacks of dyspnea, enlarged liver	98	24	200/30 13 0	1 1
						100 20 9 3	220/135 2 0
							Attacks of dyspnea have disappeared, liver not palpable
3	Aortic insufficiency, and stenosis, tabes dorsalis	59	Dyspnea with exertion, cyanosis	88	18	150/40 12 2	1 2
						68 20 5 8	210/60 2 9
							No cardiac symptoms
4	Hypertension, myocardial decompensation, auricular flutter	49	Edema, ascites, and dyspnea	64	30	145/50 15 0	1 3
						80 24 27 8	190/110 1 1
							Edema and dyspnea, no ascites

# Venous Pressure and Vital Capacity

1081

		108	24	115/90	122	12	104	24	133	120/90	12			
5	Myocardial degeneration, emphysema, bronchitis, lung infarct	64	Edema, dyspnea, cyanosis, enlarged liver				Edema, cyanosis, dyspnea							
6	Mitral insufficiency, luteic aortitis, Ecg arborization block	56	Cardiac oppression, dyspnea, liver swelling	70	18	145/75	136	27	Dyspnea and cardiac oppression absent Liver still enlarged	96	20	95	150/70	29
7	Mitral insufficiency Question of coronary thrombosis Ecg inverted T waves in leads 1 and 2, arborization block	66	Sudden attack of dyspnea and feeling of anxiety, edema	65	14	150/100	125	18	Edema diminished, dyspnea and feeling of anxiety absent at rest	60	16	28	175/95	25
8	Coronary sclerosis with angina pectoris emphysema, auricular flutter	75	Dyspnea, edema, attacks of pain and oppression in the region of the heart	80	24	145/90	178	05	Moderate exercise edema, sense of pressure in the region of the heart	88	20	58	160/100	09
9	Mitral insufficiency, auricular flutter	39	Cardiac palpitation, dyspnea and liver swelling	108	22	105/75	170	14	No palpitation, dyspnea with exertion, liver size, unchanged	92	24	182	115/85	17
10	Cardiac asthma, auricular flutter	54	Attacks of breathlessness and chest oppression	84	20	160/105			Absence of symptoms while at rest	96	18	60	150/90	20

TABLE 2

THE EFFECT OF VENESECTION ON THE VITAL CAPACITY AND THE VENOUS PRESSURE

Before Venesection					After Venesection (300 cc)			
Case	Pulse Rate	Arterial Pressure	Venous Pressure	Vital Capacity	Pulse Rate	Arterial Pressure	Venous Pressure	Vital Capacity
1	96	140/100	26 0	0 9	98	135/95	21 8	1 1
2	92	125/75	20 0	1 0	88	120/80	14 0	1 3
3	120	185/100	19 8	0 9	120	145/95	17 2	1 2

TABLE 3

ILLUSTRATIVE CASES SHOWING THE EFFECT OF UNCOMPLICATED PULMONARY DISEASES UPON THE VITAL CAPACITY THE VENOUS PRESSURES ARE NORMAL

Case	Diagnosis	Age	Weight in Pounds	Height in Inches	Venous Pressure	Vital Capacity
1	Pneumonia	28	130	66	5 0	1 1
2	Pulmonary tuberculosis	40	132	67	8 0	2 0
3	Emphysema	49	154	67	4 0	1 2

of the vital capacity Patients with pulmonary disease and normal cardiac function have only a decreased vital capacity, but if circulatory failure occurs in the course of pulmonary disease, the venous pressure is increased

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# Duodenitis, Duodenal Ulcer and Gastric Ulcer:

## Experimental Lesions Produced with Streptococci Obtained from Surgically Resected Ulcer-bearing Tissue and from Other Foci of Infection\*

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A CAUSATIVE organism of peptic ulcer was searched for in surgically resected tissue as well as in the various foci of infection and in the experimental lesions. In making cultures from the tissue, the tissue was crushed, finely macerated in a sterile mortar, with sterile sand, and then inoculated into various culture mediums. Control cultures also were made from pieces of apparently normal stomach and normal duodenal mucosa. Cultures from tonsils, extracted teeth and infected prostate glands were made. These cultural methods have been described in detail in previous publications. The cultures were then injected intravenously into rabbits in an attempt to determine their virulence and their affinity for the stomach and duodenum. In most cases two rabbits were used for each strain. In a few cases one or three rabbits were used, because of the scarcity or abundance of the supply of rabbits at the time. All the rabbits used were taken from a common stock shipped in from various neighboring states. They were maintained on a balanced

diet, and housed comfortably, and intravenous injections were given which were calculated not to exceed 1 c.c. for each 200 gm. of body weight. Usually the dose was approximately 1 c.c. for each 300 gm.

### RESULTS

*Duodenitis*—The literature concerning duodenitis without associated ulceration is meager. Hemmeter, in 1897, in a consideration of chronic gastritis, included the description of a condition identical with that which now is called duodenitis. Roeder inferred that duodenitis is relatively common. Boas and Puhl reported duodenitis associated with gastritis. Judd described a condition which he called duodenitis and which he distinguished from the usual type of ulcer by the absence of a demonstrable crater. MacCarty and Wellbrock have described the pathologic changes that take place.

Cultures were obtained from twenty-one patients who had duodenitis without ulceration, as revealed by operation. Eighteen of these twenty-one patients had one or more foci of infection which contained a streptococ-

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cus with selective affinity for the stomach or duodenum. In seventeen of thirty rabbits (57 per cent) which received injections of cultures obtained from teeth of patients, hemorrhagic lesions developed in the duodenum. Lesions of the stomach or duodenum developed also in 49 per cent of the rabbits that were given injections of cultures obtained from the tonsils, and in 28 per cent of those that received injection of cultures obtained from the prostate gland. In 53 per cent of the rabbits that were given injections of cultures obtained from surgically resected, inflamed duodenums, lesions of the stomach or duodenum developed (table 1). Altogether eighty-nine rab-

bbits were given injections, in 51 per cent of which lesions developed either in the stomach or duodenum, or both. In contrast, only one animal of the eighty-nine had a lesion of the bowel other than the duodenum, one had a lesion of the muscles and one of the liver, two animals had lesions of the kidney, three of the appendix, and six of the joints.

*Duodenal ulcer*—In a similar manner the experimental results obtained with cultures from patients with duodenal ulcer, with or without associated duodenitis, were analyzed (table 2). Ninety-three of 134 patients with duodenal ulcer had a focus of infection

TABLE 1  
LOCALIZATION IN RABBITS OF STREPTOCOCCI OBTAINED FROM CASES OF DUODENITIS WITHOUT ULCERATION

Source of culture	Number of rabbits having lesions of the											
	Rabbits injected	Stomach	Duodenum	Stomach and duodenum	Stomach, duodenum or both, per cent	Bowel	Appendix	Joint	Muscle	Lung	Liver	Kidney
Teeth	30	7	9	1	57		1	3			1	1
Tonsils	35	7	7	3	49	1	1		1	3		1
Prostate gland	7		1	1	28		1	1		1		
Duodenum	17	8		1	53			1				
Total	89	22	17	6		1	3	5	1	4	1	2
Total per cent					51	1	3	6	1	4	1	2

TABLE 2  
LOCALIZATION IN RABBITS OF STREPTOCOCCI OBTAINED FROM CASES OF DUODENAL ULCER

Source of culture	Number of rabbits having lesions of the																	
	Rabbits injected	Stomach	Duodenum	Stomach and duodenum	Stomach, duodenum or both, per cent	Bowel	Appendix	Joint	Muscle	Nerve	Skin	Eye	Lung	Gallbladder	Liver	Kidney	Heart	Spleen
Teeth	166	49	24	13	52	3	2	14	3			2	10	4	2	3	4	
Tonsils	244	55	20	49	51	1	9	10	1	1	1	3	10	5	4	14	9	
Prostate gland	219	63	25	22	50	11	9	15	2	1		1	7	5	3	17	5	1
Duodenal ulcer	46	19	11	3	72	2	1	1		1				2	1	1	1	
Total	675	186	80	87		17	24	40	6	3	1	6	27	16	10	35	19	1
Total per cent					52	3	4	6	1	1	1	1	4	2	1	5	3	1

containing streptococci with affinity for the stomach or duodenum. In 52 per cent of the 675 rabbits that received injections of cultures from the teeth, in 51 per cent of those that received injections of cultures from the tonsils, in 50 per cent of those that received injections of cultures from the prostate gland, and in 72 per cent of those that were given injections of material from surgically resected ulcers, lesions developed that resembled those in the patients from whom the injected material was obtained. In some of these cases, lesions were found in both stomach and duodenum, 52 per cent had lesions either of the stomach or the duodenum, or both. Only a comparatively small number of the animals that were given injections had demonstrable lesions elsewhere in the body, the highest number of which was in the joints.

*Gastric ulcer*—The results obtained with cultures from patients who had gastric ulcer were analyzed (table 3). Twenty-four of thirty-one patients with gastric ulcer had a focus of infection containing a streptococcus with affinity for the stomach or duodenum. As in the patients with duodenitis and

duodenal ulcer, cultures from the teeth, tonsils, prostate gland, and resected ulcers each produced lesions in the stomach or duodenum of rabbits in a high percentage of cases. Ninety-six rabbits were given injections. In 64 per cent of the ninety-six rabbits, lesions either of the stomach or duodenum, or both, developed. The highest incidence of lesions elsewhere in the body was in the joints.

*Controls*—In table 4 is shown collectively the three groups represented in tables 1, 2 and 3, together with a control group. One hundred thirty-five of 186 patients with peptic ulcer had a focus of infection harboring streptococci with affinity for the stomach or duodenum. A total of 860 rabbits were given injections of these 186 strains, and in 52 per cent of them lesions developed either in the stomach or duodenum, or both. The highest incidence of lesions elsewhere in the body was in the joints; arthritis developed in 6 per cent of the rabbits.

In the bottom row of table 4 are data on the control group which contains the results obtained with strains of streptococci isolated from patients who had no definite or recognizable

TABLE 3  
LOCALIZATION IN RABBITS OF STREPTOCOCCI FROM CASES OF GASTRIC ULCER

Source of culture	Number of rabbits having lesions of the												
	Rabbits injected	Stomach	Duodenum	Stomach and duodenum	Stomach or duodenum or both, per cent	Bowel	Joint	Muscle	Lung	Gallbladder	Kidney	Heart	Spleen
Teeth	13	8			62		1	1	1				
Tonsils	23	9	1	4	61	1	2		1	2	2		
Prostate gland	23	13		2	65	1	4	1	1			1	
Gastric ulcer	37	18	1	5	65	4			1		2	2	1
Total	96	48	2	11		6	7	2	4	2	4	3	1
Total per cent					64	6	7	2	4	2	4	3	1

TABLE 4  
LOCALIZATION IN RABBITS OF STREPTOCOCCI OBTAINED FROM CASES OF DUODENITIS, DUODENAL  
ULCER AND GASTRIC ULCER

Kind of cases from which cultures were taken	Percentage of rabbits having lesions of the														
	Cases from which strains were obtained	Cases strains from which localized in the stomach or duodenum of rabbits	Rabbits injected	Stomach, duo- denum or both	Bowel	Appendix	Joints	Muscle	Nerve	Skin	Eye	Lung	Gallbladder	Liver	Kidney
Duodenitis	21	18	89	51	1	3	6	1				8		1	2
Duodenal ulcer	134	93	675	52	3	3	6	1	1	1	1	4	2	2	5
Gastric ulcer	31	24	96	64	6		6	2				4	2		4
Total	186	135	860	52	3	3	6	1	1	1	1	4	2	1	5
		(73 per cent)													
Control group	94	11	184	9	5	1	11	5	1	1	3	8	3	2	6
		(11 per cent)													

disease, or if they were ill, had no systemic involvement. Consequently, this group contains cultures of teeth extracted for cosmetic reasons, or of teeth, or tonsils, or the prostate gland or cervix of patients with undetermined fever, insomnia, neurasthenia, or similar intangible complaints. Only eleven of ninety-four patients (11 per cent) in the control group harbored streptococci with affinity for the stomach or duodenum, whereas in 73 per cent of the cases of peptic ulcer a streptococcus having special affinity was found. Lesions of the stomach or duodenum developed in only 9 per cent of the rabbits of the control group in contrast to 52 per cent of the rabbits injected with strains isolated from patients with peptic ulcer.

In order to evaluate the significance of streptococci obtained in cultures of surgically resected tissues, four pieces of tissue from an apparently grossly unchanged stomach and duodenum were cultured. From one of the four pieces, a few streptococci were recov-

ered. However, neither this culture, nor any of the other organisms found in cultures of the grossly unchanged stomach or duodenum, produced lesions of the stomach or duodenum in nine rabbits when they were given injections of a dosage the same as or one and a half times greater than, the usual dosage employed.

In table 5, the experimental results in animals are grouped according to the focus from which the strain was obtained. The strains obtained from the teeth, tonsils, prostate gland, and resected ulcers were approximately equally selective for the stomach and duodenum, but those strains obtained from the surgically resected tissue of the duodenum and stomach had even a slightly higher selective affinity. The dominant characteristic is again evident in this table, namely, that no matter what the focus, there is a much higher percentage of lesions in the stomach or duodenum than in any other part of the body. In table 6, the results in animals are divided so that

TABLE 5  
COMPARISON OF RESULTS OBTAINED WITH STRAINS ISOLATED FROM VARIOUS FOCI IN CASES OF  
DUODENITIS, DUODENAL ULCER AND GASTRIC ULCER

Source of culture	Percentage of rabbits having lesions of the													
	Rabbits injected	Stomach, duo- denum or both	Bowel	Appendix	Joint	Muscle	Nerve	Skin	Eye	Lung	Gallbladder	Liver	Kidney	Heart
Teeth	209	53	1	1	9	2			1	5	2	1	2	2
Tonsils	302	51	1	3	4	1	1	1	1	4	2	1	6	3
Prostate gland	249	51	5	4	8	1	1		1	4	2	1	7	2
Surgically resected speci- men showing evidence of duodenitis, duodenal ulcer or gastric ulcer	100	66	6	1	2		1			1	2	1	3	3

TABLE 6  
COMPARISON OF CHANGES IN RABBITS THAT WERE FOUND DEAD WITH CHANGES IN THOSE THAT  
WERE KILLED BY AN ANESTHETIC

		Percentage of rabbits having lesions of the													
Kind of cases from which cultures were taken	Animal	Average dose, c c	Length of life, days	Rabbits injected	Stomach or duo- denum, or both	Bowel	Appendix	Joint	Muscle	Nerve	Skin	Eye	Lung	Gallbladder	Liver
Duodenitis	Anesthetized	7 4	7 3	42	57		2	10							
	Died	6 9	3 6	47	45		4	2	2				9		2
Duodenal ulcer	Anesthetized	7 5	7 6	256	40	1	2	9	1	1		1	2	3	1
	Died	7 5	4 1	419	60	1	4	1	1	1	1	1	5		6
Gastric ulcer	Anesthetized	6 4	5 8	38	63	8		10					5	5	
	Died	6 6	5 2	58	66	5		5	3				7		
Total	Anesthetized	7 4	7 4	336	42	2	2	10	1	1	1	1	2	2	1
	Died	7 3	4 2	524	59	3	4	4	1	1	1	1	6	1	5
Total				860	53	3	3	6	1	1	1	1	4	2	4

the findings in the anesthetized animals that were dispatched by anesthesia are compared with the findings in the animals that were found dead. The average dose injected was approximately the same in both groups. The rabbits that were dispatched by anesthesia naturally lived a longer time than those that were found dead. However, the percentage incidence of localization in the two groups is not at great variance. The percentage of lesions in the lungs, usually due to pneumonia, was higher among the animals that were found dead than among

those that were anesthetized, whereas the latter had a slightly higher percentage of lesions in the joints. The comparative ratios between the situation of various lesions was approximately the same whatever the manner of death. Whether the group of animals that was dispatched by anesthesia is considered alone or the group that was found dead is considered alone, or both groups are considered together, the one outstanding result is unchanged, namely, that the strains obtained from patients with peptic ulcer produced lesions more often in the

stomach and duodenum than in any other part of the body

The results of cultures obtained at necropsy were also analyzed to compare the pathogenic with the non-pathogenic strains as well as the results in the anesthetized rabbits with those obtained in the rabbits that died. In the anesthetized rabbits injected with pathogenic strains, the streptococcus was recovered from the blood in 32 per cent, from the ulcer in 67 per cent, and from the joints in 11 per cent, septicemia occurred in 11 per cent. In the animals that died the percentages were practically the same, the streptococcus being recovered from the blood in 30 per cent, from the ulcer in 67 per cent, and from the joints in 5 per cent, septicemia occurred in 11 per cent. In contrast, in the anesthetized animals injected with non-pathogenic strains, the streptococcus was recovered from the blood in only 18 per cent and septicemia occurred in 6 per cent. In those that died the blood contained the streptococcus in

26 per cent and septicemia occurred in 4 per cent. Thus there is only a slight increase in percentage of bacteremia and septicemia caused by the pathogenic strains but there is no appreciable difference between the animals that died, and those that were anesthetized. The one prominent feature is that the percentage incidence of recovery of the streptococcus was highest in the specific focal lesions.

It has been suggested that only those results should be included in the tables that had been induced by pathogenic strains which had actually produced some sort of a visible lesion in the rabbits. In order to evaluate this suggestion, all the figures were analyzed again (table 7). It is evident from the table that such exclusion raises the percentage incidence of elective localization. The percentage incidence of localization in the stomach and duodenum in cases of duodenitis is raised from 51 to 61 per cent, in cases of duodenal ulcer from 52 to 65 per cent, and in cases of gastric ulcer from 64

TABLE 7  
COMPARISON OF CHANGES IN RABBITS THAT RECEIVED INJECTIONS OF ALL CULTURES WITH  
CHANGES IN RABBITS THAT WERE GIVEN INJECTIONS ONLY OF PRIMARY CULTURES  
OF PATHOGENIC STRAINS

Kind of cases from which cultures were obtained	Strains injected	Percentage of rabbits having lesions of the												
		Rabbits injected	Stomach or duo- denum or both	Bowel	Appendix	Joint	Muscle	Nerve	Skin	Eye	Lung	Gallbladder	Liver	Kidney
Duodenitis	Pathogenic when first isolated	57	61	2	5	7					11		2	4
	All strains	59	51	1	3	6	1				8		1	2
Duodenal ulcer	Pathogenic when first isolated	482	65	4	5	7	1	1	1	1	5	3	2	6
	All strains	675	52	2	4	6	1	1	1	1	4	2	1	3
Gastric ulcer	Pathogenic when first isolated	74	70	7		9	3				5	2	3	3
	All strains	96	64	6		7	2				4	2	2	3
Peptic ulcer (total)	Pathogenic when first isolated	613	63	4	4	7	1	1	1	1	5	2	2	6
	All strains	860	52	3	3	6	1	1	1	1	4	2	1	3
Control	Pathogenic when first isolated	105	13	9	2	17	9	2	2	6	14	6	3	11
	All strains	184	9	5	1	11	5	1	1	3	8	3	2	6

to 70 per cent. Considered collectively, 52 per cent of 860 rabbits that were given injections of the various strains had lesions of the stomach or duodenum. From this figure, 860, was subtracted the number of those rabbits that had been given injections of strains that had gone through one or more animal passages, those strains that did not produce gross lesions on intravenous injection, and those that had been obtained in second cultures from a focus. This left a total of 613 rabbits that had received injections of strains that produced some sort of a lesion in at least one of the rabbits that had been given primary injections. Lesions of the stomach or duodenum developed in 63 per cent of these 613 rabbits. By this method of exclusion, the incidence of localization of strains isolated from the stomach or duodenum is increased from 52 to 63 per cent. Likewise, the percentage incidence of localization in the joints is raised from 6 to 7, in the lungs and kidneys from 4 to 5 and 5 to 6, respectively, in the bowel and appendix from 3 to 4, and the percentage incidence of the remainder of the localizations is too small to be affected. With the use of the same standard for the control group (tables 4 and 7), the percentage incidence in the stomach and duodenum was raised from 9 to 13, in the joints, from 11 to 17, in the lungs, from 8 to 14, and the percentages elsewhere were raised to a less degree. Thus, the application of this method of evaluating the selective affinity of the strains raises the percentage incidence of most of the localizations but it does not change the relative percentages ap-

preciably nor does it change the site of the localizations.

Three of the strains of streptococci also were studied to determine the possible presence of endotoxins and ectotoxins having selective affinity for the stomach or duodenum. Eighteen-hour broth cultures of the organisms were centrifugalized. The supernatant fluid was decanted and passed through a Berkefeld filter (N). The filtrate was proved sterile, and then was injected intravenously into rabbits. The sediment containing the bacteria was washed three times in sterile physiologic solution of sodium chloride, then was diluted to the original volume with physiologic solutions of sodium chloride, and was heated to 60°C for forty minutes. When it had been proved sterile, it was injected intravenously into rabbits. Thirteen rabbits were given injections in the usual manner with living broth cultures of these three strains. In nine (69 per cent) of the rabbits lesions of the stomach or duodenum developed. The highest incidence of lesions elsewhere in the body was in the kidney (30 per cent). This may be explained partly by the fact that one of the three strains used was isolated from a focus of a patient who had nephritis as well as duodenitis. Then six rabbits were given injections of washed, dead bacteria, suspended in solution of sodium chloride, and in four of the six similar lesions developed. Ten rabbits were given injections with the sterile filtrate obtained from the broth cultures of the organisms, and in nine of the ten hemorrhagic lesions of the stomach or duodenum developed. Six rabbits received injections of similar amounts of the un-

inoculated broth that had been used in making the cultures, and lesions did not develop in any. The dosage of the suspended, dead bacteria was the same as that for the living cultures. The dosage of the filtrate was slightly larger, it varied from 5 to 12 cc.

#### HISTOLOGIC CHANGES

The microscopic picture of the ulcers resected from human beings resembles that described in textbooks. The microscopic appearance of the duodenum in cases of duodenitis resembles the description of Judd and Nagel. Streptococci have been found repeatedly in the walls of resected ulcers by various investigators. However, fewer attempts have been made to demonstrate their presence in the inflamed duodenum in cases of duodenitis.

Sections of duodenal tissue from twenty-two cases of duodenitis were studied, and in seventeen of the twenty-two (81 per cent) diplostreptococci were found in the sections stained with Gram-Weigert stain. There was often the usual mixture of organisms, mainly Gram-positive and Gram-negative bacilli of various sizes and shapes, many of them spore-forming organisms on the surface of the mucosa and extending down into the crypts. Rarely they also were found in the same places in which the streptococci were found. The diplostreptococci usually were found in the mucosa, near the periphery of hemorrhages, or in the vicinity of regions of cellular infiltration. In some instances in which stippling of the serosa was noticed at the time of operation, the bacteria were found also in the depths of the muscle near the serosa. However, as a general

rule, they were not as numerous nor as deeply situated as the streptococci found in cases in which actual ulceration was present.

The experimental lesions, when situated in the duodenum, consisted mainly of submucous petechial hemorrhages, often confluent. Sometimes there was stippling of the serosa of the affected duodenum similar to that described by Judd as characteristic of duodenitis in man. When the lesions were in the stomach they usually were in the pyloric portion, or along the lesser curvature, they were less numerous, more discrete than those in the duodenum, and sometimes the hemorrhagic, necrotic center was sloughed out, producing what resembled a superficial erosion.

Microscopically, the duodenitis in animals resembled the duodenitis as found in man but it was more marked than in man. The mucosa and submucosa often were distended with the products of hemorrhage or were the site of marked cellular infiltration which frequently penetrated the muscularis, and in some instances extended to the serosa. The glandular tissue of the mucosa often was almost entirely replaced by hemorrhage and cellular infiltration.

In sections of the experimental lesions stained by the Gram-Weigert method there was sometimes a mixture of Gram-negative and Gram-positive bacilli, with a few streptococci on the surface of the mucosa. However, in the mucosa and submucosa, adjacent to regions of hemorrhagic or cellular infiltration, the streptococcus, in diplococcus form, usually was found also.

## REPORT OF ILLUSTRATIVE CASES

*Case 1 Duodenitis with hemorrhage the dominant symptom*—A farmer, aged sixty years, entered The Mayo Clinic in December, 1925, complaining of slight flatulence and occasional heart-burn but no definite gastric distress. Six years previously he had become nauseated and had vomited blood. Following this, he had been fairly well until two years before he came to the clinic when he again had vomited 1 liter of "blood" and had had tarry stools for a week. He had regained and maintained his health until eight weeks before admission, when he had another attack of hematemesis associated with dizziness and syncope. His bowels had been regular in action, his appetite had been only fair, and food had given only occasional relief.

Analysis, on the basis of 100 cc of gastric content, revealed total acidity of only 36 and free hydrochloric acid of 20, expressed in terms of cubic centimeters of tenth-normal solution of sodium hydroxide. Duodenal ulcer was diagnosed by roentgenogram. Operation revealed duodenitis without ulceration, involving the pyloric ring.

Figure 1a is a section through the excised piece of duodenum. There is no definite ulceration in the duodenum but in places there is marked cellular infiltration and edema. Figure 1b is a higher magnification of figure 1a and shows the diplococci in the tissues.

*Case 2 Experimental results obtained with cultures of resected duodenal tissue as well as of material from foci of infection*—An unmarried woman, aged thirty years, entered The Mayo Clinic in 1925 with a

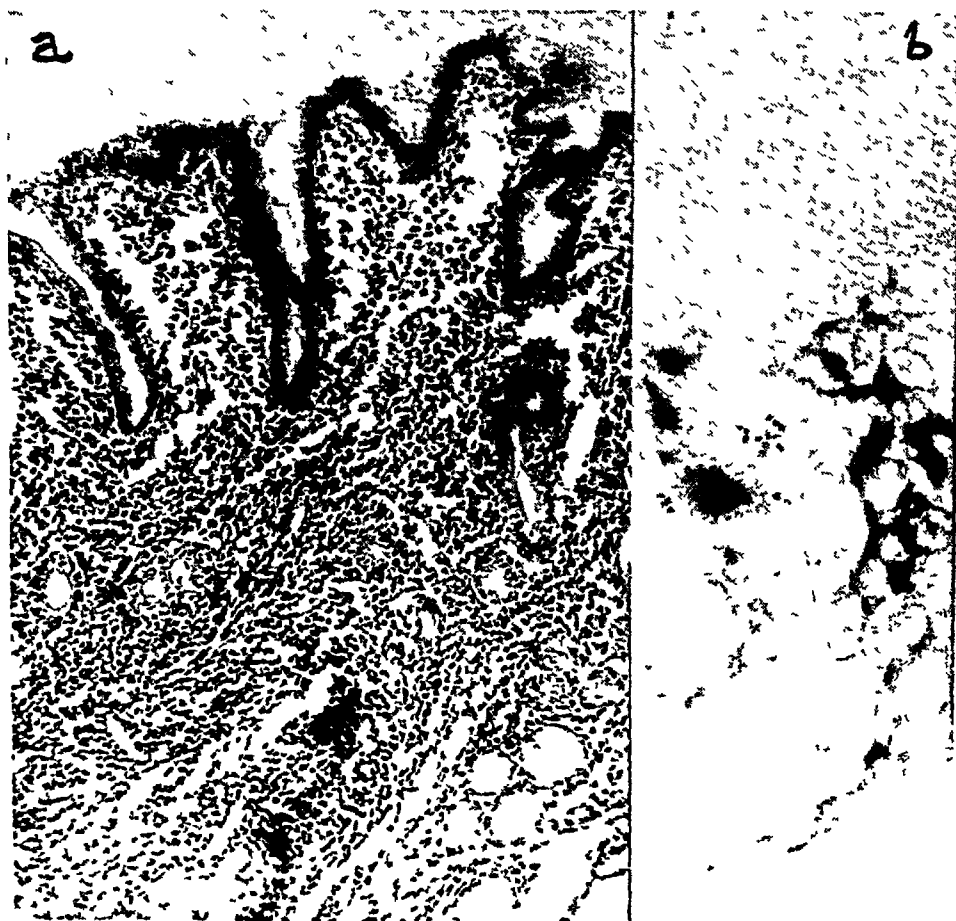


FIG 1 a, Section of surgically removed duodenum of a man. Cellular infiltration and edema characteristic of duodenitis (hematoxylin and eosin,  $\times 100$ ), b, streptococci situated in the region of the cellular infiltration (Gram-Weigert stain,  $\times 1000$ )



history of gastric distress of long standing Apples, beans, tomatoes, and similar articles of diet caused severe epigastric distress which radiated to the back and which caused residual soreness in the lower right quadrant of the abdomen This distress was relieved at times by the taking of soda or food There was no jaundice, no vomiting and no nocturnal distress A roentgenogram was positive for duodenal ulcer At operation there was found marked duodenitis and a very small area of erosion or ulceration Sections of the inflamed duodenum revealed the usual superficial cellular infiltration with occasional diplostreptococci adjacent to regions of infiltration Cultures of a piece of the inflamed duodenum, consisting mainly of green producing streptococci, were injected into two rabbits, both of which died two days later with confluent hemorrhages of the pyloric portion of the stomach, but with no other gross lesions The organism injected, a green-producing streptococcus, was recovered from the blood of one of the two rabbits and then was injected into another rabbit which was dispatched four

days later Necropsy revealed numerous discrete and confluent, irregular, submucous hemorrhages of the first portion of the duodenum (fig 2) Sections of the duodenum revealed hemorrhagic infiltration of the mucosa (fig 3) with the microbe in the depths of the mucosa near the regions of hemorrhage (fig 4)

#### SUMMARY AND CONCLUSIONS

The results given in tables 1, 2, and 3 could almost be superimposed on one another The results in cases of duodenitis and of duodenal ulcer are very similar The only important difference between them and those obtained in cases of gastric ulcer is the fact that the strains obtained from the patients who had gastric ulcer produced lesions more often in the stomach and less often in the duodenum while the strains obtained from patients who had duodenitis or duodenal ulcer produced

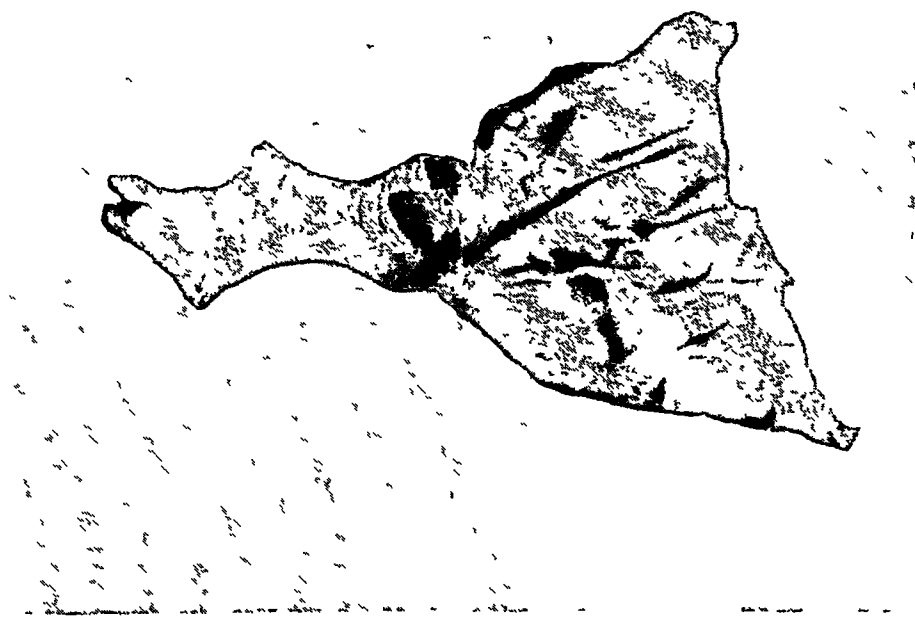


FIG 2 Submucous hemorrhagic duodenitis in a rabbit, four days after two intravenous injections at intervals of twenty-four hours, of 5 and 6 cc, respectively of a culture of streptococci in glucose-brain broth



FIG 3 Section through a hemorrhagic portion of the duodenum shown in figure 2, with multiple massive hemorrhagic infiltrations extending down to the muscularis (hematoxylin and eosin, x75)

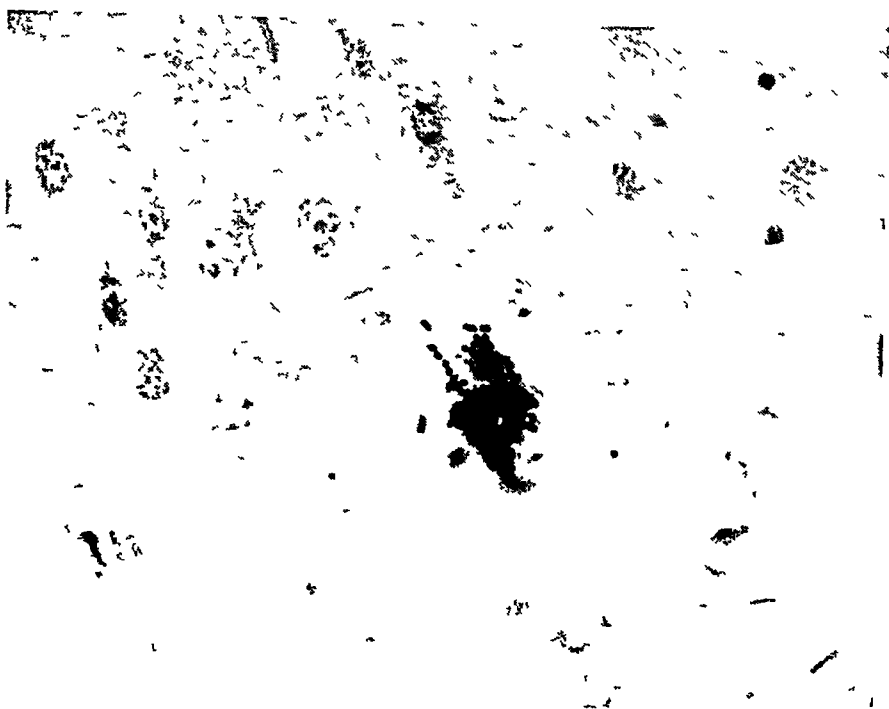


FIG 4 Diplococci near the periphery of the larger area of hemorrhage shown in figure 3 (Gram-Weigert stain, x1000)

lesions in the duodenum more often than in the stomach

Whenever the culture of the resected tissue of the stomach or duodenum consisted predominantly of green-producing streptococci, intravenous injection into rabbits caused acute hemorrhagic lesions of the stomach or duodenum in a large percentage of cases. If the culture injected consisted mainly of bacilli, or staphylococci, or other nonpathogenic organisms, focal lesions of the duodenum or stomach or lesions elsewhere in the body were relatively infrequent.

Pure cultures were not injected except as they seemed pure when isolated from the teeth or from the lesion itself. It is common knowledge that the streptococcus loses its selective affinity unless injected when freshly isolated. Consequently injection of pure-line strains obtained from infected foci are of little value since they have been on artificial mediums too long. However, a pure strain recovered from the experimental lesion, if promptly reinjected, usually localizes again electively, and culturally it coincides with one of the strains of the mixed culture originally injected. Concerning intercurrent infections, it is extremely rare to isolate a green-producing streptococcus related to such intercurrent infections which has elective localizing power.

The results from a uniform method of intravenous injection have been

analyzed from various standpoints and all the valid criticisms have been satisfactorily answered. These criticisms concerned (1) the size and number of doses injected, (2) the number of cases and controls studied, (3) the number of animals injected in each case, (4) whether the animals died from the injection or were anesthetized, (5) the intercurrent infection and experimental bacteremia, and (6) whether strains injected were pathogenic or nonpathogenic. Under these controlled conditions the incidence of lesions of the stomach and duodenum were constantly much higher than in tissues elsewhere in the body, and specific lesions produced resembled those in the patient in essential respects.

Thus a streptococcus, like the one isolated and described by Rosenow, has been consistently isolated from various foci of infection and from the surgically removed tissues in cases of duodenitis and of duodenal and gastric ulcer. It has again been demonstrated in the affected tissues of both human beings and of experimentally produced lesions, and it has been shown to have ectotoxins and endotoxins which affect specifically the mucous membrane of the stomach and duodenum. On the basis of these facts, the conclusion that this streptococcus is a causative agent in each of the three diseases studied, seems warranted.

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# The Blood Sugar During Remission in Pernicious Anemia

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## INTRODUCTION

THE similarity of the symptoms of hunger, headache, restlessness and sweating seen in early remission in patients with pernicious anemia after liver therapy and in hypoglycemia has been mentioned by Blotner and Murphy<sup>1</sup>. Investigating the blood sugar reducing properties of whole liver and liver extracts, these authors find an insulin-like, blood sugar reducing action common to whole liver and certain extracts of liver which are ineffective in the treatment of pernicious anemia. The liver extract fraction (G) of Cohn<sup>2</sup> which is effective in the treatment of pernicious anemia, they find does not exhibit this blood sugar reducing effect. In their experiments whole liver given by mouth produced a fall in the blood sugar curves after a carbohydrate test meal in normal persons and patients with pernicious anemia and diabetes, similar to that observed after the use of insulin, and lowered the fasting blood sugar values of patients with diabetes when the liver was eaten daily. From their results it might be supposed that should

hypoglycemia be an important factor in the production of hunger during early remission in pernicious anemia, hunger would appear after the use of whole liver but not after the use of an effective liver extract. Such a supposition would be incorrect for intense hunger develops as frequently after the use of an effective liver extract as after whole liver feeding. Apparently some other factor produces the hunger observed in these cases. Curtis<sup>3</sup> attributes the development of hunger symptoms to the presence of large quantities of vitamin B in liver and in effective liver extracts.

## MATERIAL AND METHODS

This study deals with the behavior of the blood sugar under fasting conditions during early remission in pernicious anemia. Frequent determinations of the amount of sugar in the blood serum taken under fasting conditions were made in eight patients with pernicious anemia under treatment with liver extract, in one patient with pernicious anemia during a spontaneous remission and in one normal person using liver extract. Usually determinations of the blood sugar values were performed at intervals of one or two days. The blood for each estimation was drawn under fasting

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conditions at 8.00 A M The method of Folin and Wu<sup>1</sup> was used in making blood sugar determinations The periods of observation extended over 8 to 27 days of liver extract treatment, being preceded with one exception by a control period in which estimations of the sugar content of the blood were made while the patient was in relapse

Lilly's liver extract No 343 (similar to the fraction (G) of Cohn) was employed in all but two patients, one patient receiving Parke-Davis liver extract, another a liver extract prepared from the livers of cod fish \*

Data on the reticulocyte percentage, the red and white blood cell counts, the amount of hemoglobin, the changes in appetite, the daily food intake in calories and the variations in the weight of these patients were also recorded

#### CASE REPORTS

With the exception of M R who was a normal person, the persons studied each exhibited the characteristic symptoms, signs, and laboratory findings of pernicious anemia The treatment given to each patient is recorded in Table No 1

No 1 Mr G F Age 38 First relapse The patient had had a thyroidectomy two and a half years before for exophthalmic goiter With development of the symptoms of pernicious anemia, symptoms of hyperthyroidism returned The basal metabolic rate, +47 before liver extract therapy, fell to +10 during remission The presence of hyperthyroidism apparently did not influence the fasting blood sugar level since this patient showed findings similar to those found in the other patients Before liver extract

was given the blood findings were R B C 860,000 per cu mm, W B C 3,650 per cu mm, Hemoglobin 19% (Sahli) After 28 days of treatment they were R B C 3,300,000 per cu mm, W B C 6,850 per cu mm, Hemoglobin 61% (Sahli) A typical reticulocyte response followed the use of liver extract, the maximum percentage of reticulocytes being 39.5% on the sixth day of treatment

No 2 Mrs M F Age 33 First relapse The blood findings before treatment were R B C 1,730,000 per cu mm, W B C 3,750 per cu mm, Hemoglobin 39% (Sahli) After 28 days of treatment they were R B C 3,470,000 per cu mm, W B C 6,550 per cu mm, Hemoglobin 68% (Sahli) A typical reticulocyte response followed liver extract treatment, the maximum percentage of reticulocytes being 17.6% on the twelfth day of treatment

No 3 Mr J K Age 64 Third relapse Before treatment the blood findings were R B C 1,100,000 per cu mm, W B C 3,750 per cu mm, Hemoglobin 21% (Sahli) After 17 days of treatment they were R B C 3,460,000 per cu mm, W B C 7,850 per cu mm, Hemoglobin 50% (Sahli) The maximum reticulocyte percentage was 25.9% on the sixth day of treatment

No 4 Mr G B Age 60 First relapse Before treatment the blood findings were R B C 1,310,000 per cu mm, W B C 4,350 per cu mm, hemoglobin 25% (Sahli) After 14 days of treatment they were R B C 2,350,000 per cu mm, W B C 6,650 per cu mm, Hemoglobin 51% (Sahli) The maximum reticulocyte percentage was 28.3% on the sixth day of treatment

No 5 Mrs M E Age 48 First relapse Before treatment the blood findings were R B C 2,490,000 per cu mm, W B C 10,250 per cu mm, Hemoglobin 55% (Sahli) After the 13 days treatment they were R B C 3,200,000 per cu mm, W B C 10,600 per cu mm, Hemoglobin 70% (Sahli) A maximum reticulocyte percentage of 7.9% occurred on the sixth day of treatment

No 6 Mr C S Age 56 First relapse During fifteen days of treatment the blood findings improved from R B C 1,370,000

\*Marine Liver Extract (G-127) prepared by White Laboratories, Inc, Gloucester, Mass

## Blood Sugar in Pernicious Anemia

per cu mm W B C 5,650 per cu mm, Hemoglobin 30% (Sahli), to R B C 2,790,000 per cu mm, W B C 7,000 per cu mm, Hemoglobin 58% (Sahli). A maximum reticulocyte percentage of 26.1% was observed on the seventh day of treatment.

No 7 Mr S M Age 68 First relapse. Before treatment the blood findings were R B C 1,120,000 per cu mm, W B C 3,600 per cu mm, Hemoglobin 29% (Sahli). A maximum reticulocyte percentage of 25.9% was observed on the fifth day of treatment. Observations on the fasting blood sugar were discontinued on the seventh day of treatment as facial erysipelas developed.

No 8 Mr M U Aged 49 Seventh relapse. Pernicious anemia was associated in this patient with tapeworm infection, the tapeworm having been removed two weeks before treatment. The initial blood findings were R B C 990,000 per cu mm, W B C 4,400 per cu mm, Hemoglobin 26% (Sahli). After 14 days of treatment R B C 2,260,000 per cu mm, W B C 5,350 per cu mm, Hemoglobin 37% (Sahli). A maximum percentage of reticulocytes of 28.0% was observed on the sixth day of treatment.

No 9 Mr M R Normal person

No 10 Mrs D R Age 40 First relapse. Without treatment the patient developed a spontaneous remission, the maximum reticulocyte percentage being 18.4% on the fourth day of observation. See Table No 2.

### THE BEHAVIOR OF THE BLOOD SUGAR DURING EARLY REMISSION

The fasting blood sugar values obtained during liver treatment from a normal person and eight patients with pernicious anemia are shown in Table 1. The values obtained in the normal person, M R, used as a control, varied from 92 to 105 milligrams of sugar per 100 c.c. of blood without liver extract treatment. During a ten day period of liver extract treatment the values obtained varied from 86 to 105 mgms per 100 c.c. of blood. These changes were not considered significant.

Fasting blood serum values were obtained before treatment in the eight patients. These values during relapse varied from 72 mgms. sugar per 100 c.c. of blood to within normal limits. The values observed before treatment were in the neighborhood of 100 to 110 mgms. per 100 c.c. of blood. Following treatment in these seven patients all exhibited a decrease in blood sugar values of from 23 to 44 points, with two exceptions, one, S M, observed an insufficient length of time to see the maximum decrease, and in the second patient, M U, the original level of the red blood count was high and the reticulocyte count feeble. The lowest blood sugar values, varying between 61 and 83 mgms. per 100 c.c., were seen from seventeen days after the beginning of treatment. If observed over an extended length of time the blood sugar values tended to rise slightly. A complete example of the change in the blood sugar values during liver extract treatment is shown graphically in Chart 1.

The patient with pernicious anemia in spontaneous remission (No 10) showed a fasting blood sugar of 133 mgms per 100 c.c. on initial estimation, the lowest value being 91 mgms per 100 c.c. ten days later, a drop of 42 points. Subsequently the blood sugar value rose to 105 mgms per 100 c.c. in this patient. (See Table No 2.)

### RELATION OF APPETITE TO BLOOD SUGAR LEVEL

In seven of the nine patients in this study the appetite was poor before treatment being c

TABLE No 1  
FASTING BLOOD SUGAR VALUES UNDER LIVER EXTRACT THERAPY  
Milligrams Sugar per 100 c c Serum

Day of Treatment*	1	2	3	4	5	6	7	8	9
	G F	M F	J K	G B	M E	C S	S M	M U	M R
—4	93								104
—3	88	87			87				
—2			100						105
—1	107				72	113	87		
0				111					92
1		90	98	88	74	111	100		
2			98	91	82		95		105
3	79	84	94	87	75	98	91		
4			106	98			96		95
5	87		98	89	79	96	83	62	
6		93	86	78			87		86
7	69	89	101	67	79	93			
8		69	87	76					99
9		83	84	76	74				
10		83	80	80					100
11	77	76	80	74	76	78			
12		67	83	82				79	103
13	80		79	80	79	72			
14		75	77	83					
15	77		80			78			
16		61	80						
17	67		83						
18		61							
19	80								
20		69							
21	69								
22	78	74							
23									
24	93	76							
25									
26	84	73							
27									
28		80							

	DIAGNOSIS	TREATMENT
*1 G F	Pernicious anemia—	Lilly's liver ext 6 vials daily 0-16 and 24-26
2 M F	" "	Marine liver ext 48 c c daily 0-22
	" "	Lilly's liver ext 3 vials daily 23-28
3 J K	" "	Lilly's liver ext 6 vials daily 0-3
	" "	Parke-Davis liver ext 6 vials daily 4-17
4 G B	" "	Lilly's liver ext 6 vials daily 0-14
5 M E	" "	" " " 4 " " 0-13
6 C S	" "	" " " 6 " " 0-15
7 S M	" "	" " " 30 " at 0 No further medication
8 M U	" "	" " " 6 " daily 0-12
9 M R	Normal control	" " " 6 " " 0-8

in the remaining two. Subjectively there was an increase in appetite in all cases after liver extract therapy. The improvement in appetite began during the first week of treatment when the percentage of reticulocytes was increasing and the amount of sugar in the blood decreasing.

The appetite, being a subjective phenomenon, is difficult to evaluate in concrete terms so the daily caloric intake and the changes in body weight were used as indices of the appetite. In every patient there was an increase in weight and food intake which began a few days after liver therapy was



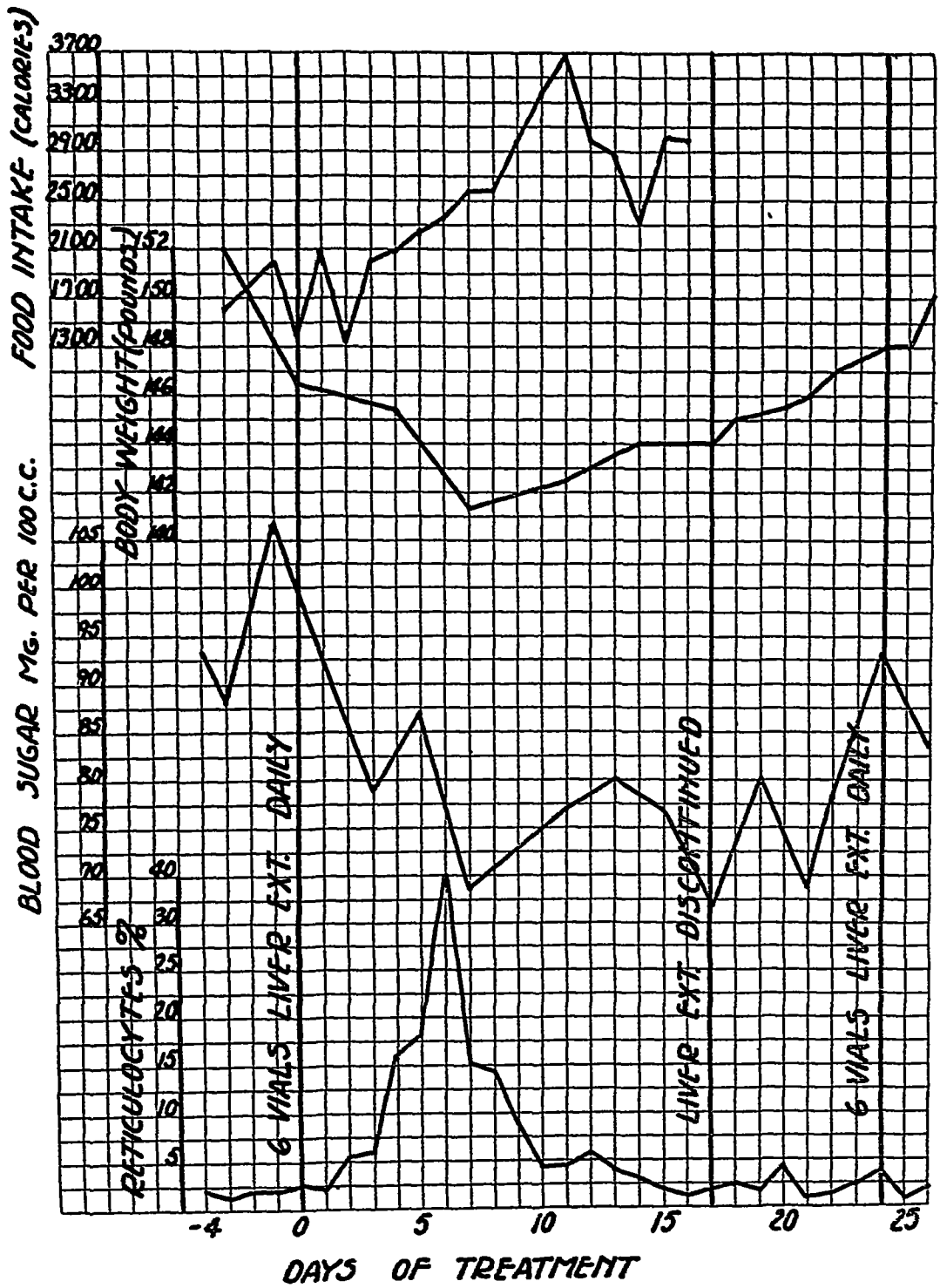


CHART No. 1  
Changes in caloric intake, weight, fasting blood sugar values and the reticulocyte percentage during liver extract treatment. (Patient No. 1)

TABLE NO. 2  
FASTING BLOOD SUGAR VALUES DURING SPONTANEOUS REMISSION  
PATIENT D R.

Days of Observation	Blood Sugar mgm per 100 c c	% Reticulocytes	Red Blood Cells Millions per cu mm
1	.	75	1 02
2		102	1 01
3	133	179	.
4		184	
5	91	119	
6		96	
7	91	96	1 64
8		73	
9	101	80	
10		68	1 56
11		55	
12	103	22	1 76

started The increase in the daily caloric intake began as a rule on the third, fourth or fifth day of treatment, the increase in weight on the fifth to seventh day of treatment The amount of sugar in the blood of these patients decreased as the caloric intake and weight began to increase The fasting blood sugar values remained low during the period of rapid gain in weight, caloric intake and appetite The increase in appetite was as a rule roughly proportional to the decrease in the amount of sugar in the blood In Chart No 1 is shown the relation between the caloric intake, body weight, fasting blood sugar and reticulocyte percentage in patient G F during the early part of a remission produced by liver extract therapy In this case the discontinuation of liver extract, was followed by a rise in the fasting blood sugar values although the increase in weight and food intake continued

The cause for the lowered fasting blood sugar values during early remission must, for the present, remain a matter of speculation The evidence at hand suggests that the decrease of the sugar in the blood is probably not produced by a blood sugar reducing, in-

sulin-like substance in liver extract Blotner and Murphy<sup>1</sup> found blood sugar reducing substances absent from liver extracts effective in pernicious anemia In the patient D R, in whom remission was spontaneous and to whom no liver material was given, the fasting blood sugar values decreased in the same fashion as in patients in whom remission was induced by the use of liver extract Patient S M. was given 30 vials of liver extract during the first day of treatment The decrease in his fasting blood sugar values continued for eight days although no further liver extract medication was given, observations being discontinued at the end of that time because he developed erysipelas These facts suggest that the fall in the fasting blood sugar values during early remission are an expression of some metabolic readjustment which accompanies remission rather than the direct effect of liver extract upon the amount of sugar in the blood. Further investigation is necessary to demonstrate the rôle which the low sugar content of the blood during early remission plays in the production of an improvement in appetite The relation of low values

of the blood sugar to remission is also interesting as various European authorities have used insulin successfully either alone or in conjunction with liver therapy<sup>5 6 7</sup> in the treatment of pernicious anemia

## CONCLUSIONS

1 A decrease in the amounts of sugar in the blood of patients with pernicious anemia takes place during early remission

2 The fall of the fasting blood sugar values appears to be related to a metabolic adjustment accompanying early remission rather than to a direct

effect of liver extract on the blood sugar level

3 The fasting blood sugar values may fall as low as 61 mgms per 100 c c of blood during early remission in pernicious anemia

4 An increase in appetite, caloric intake and body weight is associated with lowered blood sugar values during early remission in pernicious anemia

5 Further investigation is required to demonstrate the relation of the decreased blood sugar values to the improvement in appetite observed during early remission in patients with pernicious anemia.

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# Diabetic Coma: A Report of Eighty-one Instances

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THE object of this report is two-fold, first to record the cases of diabetic coma that have come under our observation since insulin, January 1923 to September 1929, and secondly to report a series of cases, the majority of which have been treated with alkali in addition to insulin

The clinical features of diabetic coma have been so thoroughly described in recent, widely published, communications that we only wish to emphasize a few of the striking symptoms. All of the cases in this group were in clinical coma, characterized by a high degree of hyperpnea, signs of dehydration, circulatory weakness, and stupor or unconsciousness. Other symptoms such as vomiting, pain in the abdomen, and hypothermia, while usually present, were not always encountered.

The patients in this series came from a mixture of sources, the majority from the private and clinic practice of one of us. Twenty-four of the patients, however, were admitted to the hospital wards without our having had any previous information as to their cases. Two of them developed coma while in the hospital, one while under treatment for diabetes and the other acute diabetes and coma while

receiving treatment for another disease. Diabetes had not been diagnosed until coma appeared in nine of the cases. Two of the patients who died were treated at home by insulin alone for a day before admission.

The causes of coma as far as could be determined were as follows: infraction of dietary rules, 41 instances, the omission of insulin, 13 instances, and infection, 12 instances. Insulin was omitted for various reasons—vomiting, the extraction of teeth so that the patient could not eat, the breaking of an insulin syringe and failure to have another in reserve, self experimentation, carelessness and indifference. In 1927 within a period of ten days, four cases of coma, precipitated by the abrupt withdrawal of insulin, were seen, two having omitted but two doses. This is an unpremeditated experiment, as convincing as those of Hedon<sup>1</sup> who produced typical diabetic coma in partially depancreatized dogs by getting them in good flesh by the use of insulin and then suddenly withdrawing it. Since this experience we have written to all severe diabetic patients warning them of the danger of omitting insulin for any reason except on the advice of their physician, and, judging from the number of types of coma cases that we have seen in the past year, the warning has been heeded. The infraction of dietary rules will probably always be the greatest cause of coma, we believe with Joslin that the frequent

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periodic visits to a physician or clinic is the most efficient safeguard that a diabetic patient may have. Infections should not precipitate coma if the patient and the physician realize their importance to the diabetic, under such circumstances the insulin should usually be increased, the diet reduced and the infection be treated radically if possible. In short it would appear that the majority of instances of coma could be eliminated, except in the small percentage who, because of indifference, will break diet, the severe diabetic patient whose coma threshold is very low, and lastly in the patient who is improperly carried through an infection.

Eighty-one instances of coma in sixty-three patients comprise this group. Of these, forty-five were females and eighteen males. Seven had more than one attack and three were common offenders, two with five attacks and one with six. None of the patients with repeated attacks were lost. Fifteen of the instances occurred in children under 15, none were fatal. Ten patients died either during or following the attack, these will be discussed later. Of the remaining fifty-four we have information of forty-four, six of them have died since leaving the hospital.

#### LABORATORY EXAMINATIONS

*Blood sugar.*—This was obtained in sixty-four instances before treatment was started. The maximum was 1320 mgms. and the minimum was 266 mgms. It exceeded 400 mgms in fifty-three instances, 83 per cent.

*CO<sub>2</sub> capacity of the plasma.*—We were able to get this determination in

fifty of the cases before insulin was given. The variation was between 3.5 and 15 mm, thirty-one of them being less than 7 mm, 62 per cent.

*Blood urea nitrogen.*—This was studied during the coma phase in forty-one of the eighty-two cases, the figures varying between 81 and 123 mgms per 100 cc. Thirty-three of these exceeded 20 mgms, 75.5 per cent.

*Leucocytes.*—A white count was obtained upon admission in forty-seven of the cases. The variation was between 6,000 and 44,000 per cu mm. The count exceeded 15,000 in thirty-five or 74 per cent of the cases.

*Treatment.*—While treatment would be unsuccessful in every case of true diabetic coma without insulin, other measures are equally important and patients do not respond satisfactorily when insulin alone is used as was demonstrated in two of our patients who were treated at home before being admitted to the hospital. As soon as the diagnosis was established, which in the usual case requires but a glance, insulin was given, generally 50 units. The ambulance doctor was always equipped to give insulin at home. When it was known that a patient was expected, the ward nurse, house physician, laboratory and ambulance doctor were notified and, if possible, the home was requested to have extra blankets and hot water bottles ready. The patient was placed in a warm bed and disturbed and uncovered only as necessary. A hypodermoclysis of 1000 cc of normal salt solution was given. An enema was given if the bowels had not moved that day and in the great

majority of cases alkali in the form of sodium bicarbonate, 5 per cent solution, was given by proctoclysis. In this group it was administered to sixty-three or 76 per cent. The total dose for the first twenty-four hours never exceeded 40 grams and the average dose was about 30. Frequently if no vomiting was present and the patient was able to swallow it was given by mouth or through the stomach tube after lavage. We found it necessary, however, to wash out the stomach but rarely as it usually is quite an arduous procedure for a coma case who has such a weakened circulation. Sodium bicarbonate was given intravenously in but two cases and lately it has been abandoned altogether under ordinary circumstances. Insulin, after the initial dose, was given in varying doses, 10 to 30 units, every two to four hours until the Benedict test began to retain some of its blue color. As a rule no carbohydrate was given until this condition was obtained, when orange juice was attempted. If vomiting was still present, glucose in a 5 per cent sterile solution was given subcutaneously in doses of 500 cc every six or eight hours, preceded by a fair dose of insulin. The average insulin dosage for the first twenty-four hours was 150 units, some requiring three times that amount while others responded to one-half that dosage. This requirement did not appear to have any direct relationship to the height of the blood sugar, the  $\text{CO}_2$  capacity of the plasma, the degree of leucocytosis, or the blood nitrogen, although we usually expected a patient with extreme hyperglycemia to tolerate more insulin; when the initial blood

sugar was low, carbohydrate was given with the insulin. Frequent urine examinations, so that the progress may be watched and the insulin-carbohydrate dosages estimated, are important. When possible, the urine was examined by the nurse before each insulin administration and if the urine was nearly sugar free the interne was informed.

In the earlier years all patients were catheterized if they could not void voluntarily, but in the past two years this practice has been given up, unless the bladder is distended, because two patients developed urinary tract infection following repeated catheterizations, which interfered with convalescence. At the present time we make frequent blood sugar examinations if it is impossible to get urine specimens for testing. It is quite safe usually to rely upon experience alone as insulin reactions during the coma phase are exceedingly infrequent.

Nearly every coma manifests a degree of circulatory insufficiency, hypotonia, tachycardia and acrocyanosis. The exact nature of this disturbed function is not understood; dehydration and toxemia caused by acidosis have been blamed, nevertheless caffeine sodium benzoate or a reliable hypodermic digitalis preparation have been used in our cases. It is impossible to determine their efficacy as one or the other has been used in all cases, recently, however, digitalis has been routinely employed and caffeine sodium benzoate has been reserved as an emergency stimulant. The fluid intake in the first twenty-four hours was from three to six liters and as a large amount of this was retained, it

gives one an idea of the tremendous dehydration present in these cases. After the emergency measures were well started the patient was carefully examined for infection and appropriate special treatment instituted where necessary. If there was need for the evacuation of pus, it was done immediately. The average case received a diet of orange juice on the second day, milk on the third and fourth, then a soft diabetic diet and an ordinary diabetic diet usually at the end of a week.

The urine of our patients was frequently examined for albumin and casts as they are usually present in the early stages. The blood nitrogen in the majority of patients upon whom it was determined was found elevated early, and patients whose convalescence was unexplainedly protracted often had an increase in blood nitrogen after the coma phase had passed. Oliguria which we felt was caused by renal insufficiency was seen in a few cases.

The treatment of coma, while it may be carried on successfully at home with the assistance of nurses, is much more advantageously handled in the hospital, where a coordinating organization exists.

#### COMPLICATIONS IN PATIENTS WHO SURVIVED COMA

Mild upper respiratory tract infections	6
Otitis media	3
Pregnancy with caesarean section	1
Abscess of leg, acute nephritis with urinary suppression	1
Measles	1
Pulmonary tuberculosis	2
Acute salpingitis	1
Empyema of the antrum, perirectal abscess	1
Acute tonsillitis, furunculosis	1
Erysipelas	1

Cysto-pyelitis	4
Abscess of the jaw	1
Miscarriage after coma phase	1
Cellulitis of the foot	2
Arthritis	1
Lobar pneumonia	1
Acute nephritis, urinary suppression	2

Complications, some of serious nature, occurred in about 50 per cent of our cases. Three cases of acute nephritis and oliguria or suppression which have been published in a separate article occurred. One of our patients had a Caesarean section during coma and improved as soon as the uterus was emptied. Our case of lobar pneumonia and coma in a girl of thirteen, with very severe diabetes, had a stormy course for several days, but finally recovered after a protracted febrile period caused by delayed resolution.

#### ABSTRACT OF CASES THAT DIED

*Case 1*—A woman of 27 years. Coma developed a week after the omission of insulin. She was in that state twelve hours before admission during which time the only treatment was 200 units of insulin. Extreme circulatory weakness developed in the interim between when she was seen at home and her admission, at which time it was impossible to feel the pulse or to measure the blood pressure. Blood sugar on admission, 500 mgms. Heart rate, 160. Cyanosis and dehydration, extreme. Respirations, 60. During the twelve hours that she lived, 100 units of insulin, 4500 cc of fluid in the form of salt solution both subcutaneously and intravenously, glucose, 5 per cent solution, both per rectum and subcutaneously, and sodium bicarbonate, 35 grams per rectum in a 5 per cent solution, were administered. The stomach was lavaged. Digitalin, 9 ampules, (0.8 gram of powdered digitalis) were given subcutaneously. Oxygen was administered with the McKesson apparatus for several hours before death. No necropsy permitted.

*Case 2*—A woman of 52 years. The patient was admitted to the hospital in coma. Blood sugar, 490 mgms per 100 cc,  $\text{CO}_2$  capacity of the plasma, 7 mm, urea nitrogen in the blood, 27 mgms, leucocytes, 26,000 with 92 per cent of polymorphonuclear cells. In the first twenty-four hours 130 units of insulin, 3000 cc, of fluid, and caffeine sodium benzoate, 7 ampules were given. The patient received no alkali. A decubitus ulcer on the buttock appeared on the sixth day. Recovery from coma was complete and the diabetes was gotten under control but on the seventh day fever and a chill developed which was followed by increasing signs of cardiac failure. The leucocyte count again rose to 28,000. No positive clinical diagnosis was made and the patient died on the thirteenth day. Necropsy showed septico-pyemia, purulent myocarditis and pericarditis, hepatitis and nephritis.

*Case 3*—A man of 30 with a gangrene of the leg entered the hospital in coma. Blood sugar, 500 mgms,  $\text{CO}_2$  capacity of the plasma, 5 mm, blood urea nitrogen, 36 mgms, leucocyte count, 21,000. During the first twenty-four hours he received 130 units of insulin, 2000 cc of fluid, 35 grams of sodium bicarbonate and caffeine sodium benzoate, 0.6. He was catheterized. He responded well to treatment with the exception that he was stuporous most of the time, the blood sugar remained fairly normal and the urine was sugar free. His leg was amputated on the tenth day. An insulin reaction occurred on the eleventh day because of refusal to take food. On the twelfth day he developed high fever and respiratory difficulty and died within a few hours. There was no necropsy but the diagnosis of probably pulmonary thrombosis was made. The arteries of the amputated leg showed arteriosclerosis especially in the distal portions.

*Case 4*—A woman of 40 years, entered the hospital with facial erysipelas and coma. Blood sugar, 532 mgms,  $\text{CO}_2$  capacity of the plasma, 7 mm, leucocyte count, 9,800 with 79 per cent of polymorphonuclears. She received 165 units of insulin, 40 grams of sodium bicarbonate, 0.7 powdered digitalis, and 8,000 cc of fluid in the first twenty-four hours. During the following

twenty-four hours she received two 10 cc ampules of Birkhaug's anti-streptococcus serum. The blood sugar came to normal and the urine became free of sugar but the patient did not improve, except that the hyperpnea disappeared and the stupor diminished. The temperature remained high,  $102.0^\circ\text{F}$  to  $104.0^\circ\text{F}$ , and the erysipelas extended. She died on the sixth day.

*Case 5*—A farmer of 51 entered the hospital in coma. The blood sugar was 432 mgms,  $\text{CO}_2$  capacity of the plasma, 7 mm, blood urea nitrogen, 35 mgms, and the leucocyte count, 10,000. His pulse rate was 130 and the blood pressure was 130 systolic and 60 diastolic. He received 140 units of insulin, 35 grams of sodium bicarbonate and 4,000 cc of fluid in the first twenty-four hours. He responded well to treatment but had an insulin reaction thirty-six hours after admission so that it was necessary to give glucose intravenously. At the end of forty-eight hours he experienced a sudden severe attack of dyspnea and died within a few minutes. The post-mortem blood sugar taken immediately was 104 mgms and the urine obtained by catheterization showed a trace of sugar.

*Case 6*—A woman of 40 who had been ill for four days with vomiting and pain in the abdomen before admission. She had received no specific treatment except 70 units of insulin shortly before her admission. Hyperpnea and dehydration were marked. She received 150 additional units of insulin, 40 grams of sodium bicarbonate, 11 ampules of digitalis (10 powdered digitalis), 7 ampules caffeine sodium benzoate, and 4,500 cc of fluid during the first twenty-four hours in the hospital. The following morning the blood sugar was 274 mgms, and the  $\text{CO}_2$  capacity of the plasma was 23 mm. The leucocyte count on admission was 19,000. The hyperpnea and the evidence of dehydration disappeared but the patient remained stuporous. She developed fever on the second day which became very irregular and reached  $104.0^\circ\text{F}$  on the seventh day. The leucocyte count dropped to 3,800. There was no satisfactory explanation for the fever. The spinal fluid was negative but unfortunately a blood culture was not done. The



blood urea nitrogen rose to 66 mgms. and the urine showed increasing albumin and casts. She died on the eighth day.

*Case 7*—A woman of 49 omitted insulin while on a three day automobile trip. She was admitted to the hospital in coma. Pronounced circulatory failure and cyanosis were present. Pulse, 110, rectal temperature 96.0°F, blood pressure 96 systolic and 60 diastolic, blood sugar 460 mgms. During the eight hours before she died she received 80 units of insulin, fluids, 2,400 cc, caffeine sodium benzoate 10 and sodium bicarbonate, 50. The patient died within a few minutes following the intravenous administration of 125 cc of 5 per cent glucose and 3 per cent sodium bicarbonate solution.

*Case 8*—The patient, a woman of 47 years, was known to have had hyperthyroidism and an increased basal metabolism prior to her admission in coma. The pulse was 166, rectal temperature 96.4°F, blood sugar 400 mgms, and the CO<sub>2</sub> capacity of the plasma was 9.5 mm. The patient was given 165 units of insulin, sodium bicarbonate, 3 per cent solution and glucose, 5 per cent solution intravenously. Her blood sugar five hours later was 500 mgms. She died without having shown any signs of improvement ten hours after admission.

*Case 9*—A woman of 39 entered in coma. Her pulse rate was 160 and the rectal temperature was 101.0°F. She received 140 units of insulin, 2,300 cc of fluids of which 800 cc was a 3 per cent sodium bicarbonate solution given per rectum, and caffeine sodium benzoate, 20. Her blood sugar was 308 mgms the morning following admission. The symptoms of acidosis improved but the pulse rate remained high. Hyperthyroidism was suspected because of extreme restlessness, tachycardia, flushing of skin, precordial pain, and sweating. Lugol's solution, 20, was given. Her circulation failed rapidly at the end of fourteen hours, which event came on with surprising rapidity and which in our hands was unresponsive to treatment. She became moribund in sixteen, and died eighteen hours after admission. Adrenalin chloride was given subcutaneously and also into the heart.

*Case 10*—A stout woman of about 50 was admitted to the surgical service because of alleged osteomyelitis of the femur. The only history obtainable was that she had been ill about five days. She was extremely hyperpneic, dyspneic and cyanotic. There were signs of consolidation of the base of one lung. Diabetes was suspected because of hyperpnea and coma. The blood sugar was 400 mgms, and the leucocytes were 18,000, rectal temperature, 103.0°F, pulse rate, 120. She received 70 units of insulin, caffeine sodium benzoate, 20, fluids, 2,000 cc, but no alkali. Her condition which seemed hopeless from the first became gradually worse and she died in eight hours.

It will be seen that most of these cases died of irremediable complications; five of them died after coming out of coma. Infection probably precipitated the coma in cases 3, 4, and 10. It appears that only cases 1, 8, and 9 died of uncomplicated coma, but as necropsies could not be secured, we cannot be certain. In cases 1 and 8 there was extreme hypotonia which did not improve with treatment and in case 9, a woman of 39 with suspected hyperthyroidism died unexpectedly. Serious circulatory disturbances are so common in diabetic coma that Dr Werner J. Rose has made an electrocardiographic study of a group of these cases. He found no electrocardiographic indication that there was myocardial damage.

#### INCIDENTAL FINDINGS

Five cases showed a rather paradoxical finding in that they were complicated by infection and yet failed to develop leucocytosis as is the rule in an uncomplicated coma case, one with extensive lobar pneumonia never exceeded 10,000 per cu mm, the highest count in one with pyelitis was 5,300,

one with an abscess of the jaw had but 13,000, another with erysipelas had 10,700, and a child with measles had 5,000. Two patients developed clinical paroxysmal auricular fibrillation during the coma phase; both recovered.

Abdominal pain of varying degrees was found to be an exceedingly frequent early symptom of coma. It was occasionally severe enough to prompt the use of morphine and in several instances it was sufficiently misleading to cause the physician to diagnose an intraabdominal lesion requiring surgical treatment. We had no explanation for this pain but apparently it is directly associated with the acidosis as it disappears soon after the institution of treatment.

#### THE USE OF ALKALI

The value of alkali in the treatment of diabetic coma is still in a controversial state. Joslin<sup>2</sup> has amply proven that coma may be effectively treated without its use. In his recent report of 105 instances of coma in 90 patients, there were 14 deaths, 2 were uncomplicated, 5 were complicated and 7 died from complications within a short time after recovery from coma had taken place. Sodium bicarbonate was given in 76 per cent of the instances in our cases, the total dose for the first twenty-four hours never exceeded 40 grams and it was rarely given on the second day. The manner of administration was usually by proctoclysis, occasionally by mouth and in two instances small amounts were given intravenously. The average case of diabetic coma apparently does not require alkali to make a satisfactory re-

covery but it has been our clinical impression that cases respond faster and that they are more readily relieved of hyperpnea, which is often distressing, when alkali is used. In cases accompanied by nephritis, urea retention, and oliguria or suppression of urine, such as were reported by Bowen and Beck<sup>3</sup> in 1925, the employment of sodium bicarbonate seems to be justified, as in these cases improvement did not take place until alkali was given. John<sup>4</sup> has recently reported a similar experience in one case. There does not appear to be any sound contraindication to its use except the fear of alkalosis, this did not occur clinically in our cases, but care was taken to place a "stop order" on the dosage. Hartmann and Darrow<sup>5</sup> have recently reported a comparative study of the composition of the plasma in severe diabetic acidosis and the changes taking place during recovery in cases treated with insulin, water and carbohydrate, but without salt or alkali, cases treated with insulin, carbohydrate and Ringer's solution but without alkali, and cases treated with insulin, carbohydrate, Ringer's solution and alkali. They find that the base-bicarbonate and hydrogen ion concentration were restored slowly by the use of insulin and water and it is their belief that salt solution adds little toward the early recovery of plasma bicarbonate. They state, however, that sodium bicarbonate when given with insulin, carbohydrate, and salt solution, may provide a rapid, safe and complete relief from acidosis. They too comment on the rapid restoration of normal breathing following the administration of alkali as we have observed.

## SUMMARY AND CONCLUSIONS

Diabetic coma constitutes an acute metabolic disturbance and like all accidents is largely preventable. When treated as an emergency nearly every patient, unless his case be complicated by a serious disease, should recover unharmed and often benefited in that he has learned a valuable lesson. It does not appear that coma can be entirely eradicated as diabetes often is not diagnosed until coma appears, also a certain percentage of patients even if they be carefully taught are normally careless and indifferent and some severe diabetic patients, even though they take good care of themselves, may easily be swung into coma by a trivial circumstance.

We wish to emphasize abdominal

pain as an exceedingly frequent early symptom of impending diabetic coma.

Death from uncomplicated coma occurred as far as could be determined in three of our sixty-three patients. In all cases there was evidence of circulatory failure, hypotonia, tachycardia and cyanosis. The nature of this is not understood, but it probably is a result of acid intoxication, as in our experience cases that were treated early did not manifest this disturbance.

The use of sodium bicarbonate, 40 grams or less during the first twenty-four hours, in addition to the insulin, salt solution and water appears to be harmless and in some cases we believe that alkali is decidedly beneficial. Its use appears to shorten the period of acidosis.

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# "Arbitrary Period of Disability" As a Mode of Settlement in Compensation Claims

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## DEFINITION

**T**HE period of disability as it is conceived in medico-legal terminology is that length of time during which an employee in any industry is unable adequately to perform any gainful work. The disability may be total such as might prevent the attendance of the employee at his place of occupation, or partial, disabling him from doing the usual amount or type of work per hour or day.

Besides these two, there are, of course, variations in the capacity of any worker that depend upon many other diurnal or intermittent factors, such as fatigue, general state of health, state of mind, et cetera. These, however, have no bearing on the compensation aspects. The gradation between these as well as between total and partial disability, and particularly the progress from partial disability to full capacity for work is almost always slow.

## ARBITRARY PERIOD OF DISABILITY

It is therefore quite important to determine as nearly as possible the beginning and end of the periods of partial and of total disability. This is often difficult to do. From objective findings alone, it is not usually advisable to

make a prognosis of the duration of disability. The subjective complaints of patients in these cases come into such important play that they make the determination quite indefinite. There may exist an independent disabling malady that overshadows the accidental illness and prolongs the patient's disability.

On this and other accounts, in a large number of cases requiring the consideration of these questions, it is of great assistance to apply a principle that may be called "an arbitrary period of disability." This must embrace the probable duration of all effects of the alleged accident, particularly in retrospect, after the patient has recovered from them. It must also take into account the patient's mental attitude, as well as that of the insurance carrier, toward the liability aspects of the case. The state of mind adumbrating the patient's physical condition frequently demands a summary settlement, if it is at all equitable. The confirmatory opinion of the patient's attending physician is of invaluable assistance in such settlement. Only then does the patient reconcile himself to the prospect of resuming his work.

The length of the arbitrary period of disability, i.e., the exact moment of its termination need not be decided

with precision. It often is satisfactory to the patient and the carrier if the period of disability, both partial and total, is considered to lie within a liberal time allowance. The application of this principle will be exemplified later in the consideration of particular cases.

#### CLASSIFICATION

The determination of an arbitrary period of disability as a help in the liability settlement of compensation claims is required particularly in certain types of cases. These may be listed as follows:

- 1 Where the disability depends on subjective complaints alone, as in cases of cerebral concussion, heart strain, and some other more obscure clinical conditions.
- 2 Where the objective findings have abated and the subjective complaints persist, as in cases of gas poisoning, lead poisoning, etc.
- 3 Where the question of temporary aggravation is plausible, although an underlying progressive condition exists, such as pulmonary tuberculosis, thromboangitis obliterans, hyperthyroid states, organic heart disease, and other progressive conditions.
- 4 In slow healing injuries of the viscera, especially lung injuries.
- 5 In the milder forms of post-traumatic hysterias or traumatic neuroses.

#### DISCUSSION OF CASES

1 *Where the Disability is Essentially Only Subjective*—In the consideration of cases presenting very few or no objective signs, the credibility of

the patient is an important factor in establishing the period of disability. The examining physician's impression is gained mainly from the medical history given by the patient—its consistency, the lack of exaggeration,—and from frank responses during the physical examination. In general, a judgment must be based on the underlying personality of the claimant, together with the essential conditions of his employment and his compensation claim.

Of course, cases of malingering, if diagnosed, are naturally dismissed from consideration. However, patients who exaggerate because of a natural tendency or because of their mental attitude to the particular accident still require the equitable adjustment of their compensation claims. In these cases, the application of an arbitrary period of disability will not be so liberal as in those cases where the symptoms have a definite organic basis.

The following case is an example of this group.

Erna G., 34 years old, fell down twelve steps of a stairway and regained consciousness after being removed to the medical department at the place of the accident. She had dull pain in the back of the head, but spent two weeks in the country without symptoms. The headaches persisted, recurring at times quite severely, with nervousness and hysterical crying and laughter. The patient gave a history of occasional headaches and bilious attacks which were present before the accident and were associated with hysterical manifestations. She complained, however, of insomnia and restlessness at night, palpitation at times, and slight loss of weight, but she worked steadily after her return from vacation.

Physical examination, 6 months after the accident, was negative except for a hysterical restlessness of her hands, biting of her fin-

ger-nails, inconstant digital tremor, and hyperactive tendon reflexes. The basal metabolic rate was normal.

*Discussion.*—A certain amount of cerebral concussion was conceded to have occurred at the time of the patient's accident. But the previous history in this case lays the background upon which we can interpret the nervous twitchings and hysterical manifestations that were noted in the physical examination and the post-accidental complaints. By the studies made in this case, we were able to exclude hyperthyroidism, cerebral disease, or other organic neurological changes that might otherwise be attributable to the accident.

We assumed that the accident aggravated the patient's prior nervous condition, exaggerating her subsequent symptoms. The effects of the accident were considered relatively temporary, and an arbitrary period of disability was satisfactorily applied in the settlement of this case.

### 2 *Where Subjective Complaints Persist.*

—The general question in these cases follows the same line of argument as in the previous group. In these, however, full allowance for disability must be made for the period during which objective findings were positive. The arbitrary period follows only subsequently. His symptoms and complaints persist and his disability must be continued until it is obvious that no further disability can be attributed to the original accident. In these cases, when the patient returns to work, an allowance must be made in retrospect up to the time when his symptoms have completely subsided.

This is illustrated by the following case.

Sidney F., a young linotyper, 29 years of age, when he was examined by us complained of symptoms of plumbism of two years' duration. He began to have cramp-like abdominal pain associated with nausea, and a diarrheal stool almost daily on arising. For six months, he also felt weakness of his hands and wrists in working the linotype machine. He noticed increased pallor and became easily fatigued.

Examination showed a moderate degree of secondary anemia with slight variation in the shape and size of the corpuscles, but there was no granular basophilia. Some of the peripheral vessels were tortuous. The physical findings were otherwise negative.

*Discussion.*—The patient presented the early symptoms of plumbism. After a time spent away from his occupation, he was advised to undertake a less hazardous occupation for so young a man. His symptoms disappeared and an arbitrary period of disability was suggested and accepted in settlement of his claim.

### 3 *Where Temporary Aggravation Has Occurred of an Underlying Progressive Disease.*

—These cases form by far the largest group amenable to settlement of their claim by the "arbitrary period of disability." Determining the amount of liability in cases of this character involves the consideration of certain general factors. These are:

- a The competency of the accident as a producing cause of the condition or disease in question.
- b Its competency as a cause of aggravation, if the disease pre-existed.

- c The length of time during which the effects of the alleged accident caused aggravation
- d The effects of complications and sequelae of the accident
- e The amount of total disability and of partial disability during that period
- f The curability and termination of the underlying progressive disease or condition.

Some of these themes must often be decided quite arbitrarily

The relationship between an accident and an ensuing disease may be considered only in a general way. When a grave accident is followed by a rapidly advancing and marked state of thyrotoxicosis, for instance, the two may be causally related. But even in such an instance, the fact of sequence does not absolutely prove causal relation. There may be simultaneous emotional or nervous disturbances, quite unrelated to the accident, that may have caused the thyroid condition. However the benefit of the doubt in such an instance can be given the patient, and the disability attributed to the accident. This does not, of course, apply in infectious conditions where the agent is bacterial and was not introduced by the accident.

The competency of an accident as a cause of aggravation is not easily determined. In most cases, some amount of aggravation may be allowed to an accident, even if there be only superimposed nervous effects. In the legal hearings of these cases, there is often introduced a great deal of quasi-medical terms which confuse the issue and allow only for an equivocal consideration of the cases. Such terms

as "lowered resistance," "diminished vitality," and "shock" are used and elaborated upon at great length without any scientific conception and without any helpful value. In some cases, this question will require more ample discussion. These we shall take up under the various headings of the underlying conditions. The other factors to be considered are also best left for the various diseases where they will be more pertinently amplified.

*Pre-existing Pulmonary Tuberculosis*—Medical opinion is apparently divided as to the possibility of accidental aggravation of pulmonary tuberculosis. One school holds that in order that the accident must bear a relationship to the pulmonary tuberculosis, the latter must be present in the region of the injury to the chest. Tuberculosis in the opposite lung, or even in a distant region in the same lung cannot be attributed to the accident unless some clinical correlation is apparent between the place of injury and the tuberculous focus. This holds true for either activation of a dormant process, or aggravation of an active lesion.

The other school believes that any physical shock or injury, either in the chest or elsewhere in the body, may and frequently does so disturb a latent or inactive focus of disease in the lungs that active tuberculosis ensues. It is by no means necessary that such an injury or blow should be on the chest itself. When the injury does occur to the chest, the likelihood of stirring up such an old latent condition is greater. The shock occasioned is transferred with almost the same de-

gree of violence to the opposite side of the lung as it is to the lung actually affected. Many instances of such contra-lateral lesions are on record, both in the chest and in the skull. They are technically known as the effect of "contre coup."

In both aspects of this subject, the time relationship between the accident and the clinical evidence is important. The effect of trauma is promptly evident in these cases. The symptoms develop within three months after the injury. If the symptoms of tuberculosis do not develop until after six months, there is no reason to suspect that the injury has any relationship to such tuberculosis. Some experts define the time limits even more closely, confining the accidental effects only within a period of two or three months.

Peter K., a man of 59 years, while lifting a heavy wooden door, felt a sudden sharp pain in the left mammary region with cutting sensation upwards. He became very pale and perspired profusely, but did not faint. The pain lessened in severity, but after resting fifteen minutes, he expectorated a small amount of fluid and slightly frothy blood. Slight blood-streaking of the sputum recurred a few weeks after the accident. There were no other developments but moderate cough and expectoration and considerable loss of weight.

Physical and roentgenographic examination showed extensive infiltration, fibrosis, partial consolidation, and small and large cavity formations throughout both upper lobes, more marked on the left side. There was pleural thickening, more marked on the left side. There was corresponding dulness and bronchial breathing and crepitant rales over the involved areas. The heart borders merged with the pulmonary dulness and therefore were not well-defined. The sputum showed the presence of tubercle bacilli.

Besides, the patient had moderate arteriosclerosis and albuminuria.

*Discussion*—From the history of slight hemoptysis immediately following the accident, and from the positive physical findings of advanced pulmonary tuberculosis, we may attribute the patient's pain following effort to the tearing of a capillary or of a pleural adhesion.

The claimant had a well advanced pulmonary tuberculosis that dated back, doubtless before the alleged injury. The only consideration that remains is of aggravation as a result of the exertion. It is probable that a temporary localized aggravation occurred, since the symptoms and disability started immediately at that time. However, the period over which such an aggravation is active can and must be determined entirely on an arbitrary basis.

We consider that about six months is a liberal time to allow for the effects of the aggravation in this case to subside. The condition otherwise, naturally, progresses uninfluenced with little prospect of cure. Under ideal conditions, of care, rest, good food, and fresh air such as may be obtained in a sanatorium, the tuberculosis may reach an arrested stage.

We therefore believe that an arbitrary period of six months' disability may be allowed as attributable to the aggravation produced by the alleged accident in this case.

Abraham G., a janitor 37 years old, lifted a barrel of ashes weighing 100 lbs and immediately felt a sudden tearing or aching pain in the upper right chest, both in the front and back of the right shoulder. He coughed with increasing pain and the expectoration of a small amount of pink-



colored fluid blood. A few hours later, the patient expectorated a glass of fluid blood and small amounts for two weeks after. For the following six months, his only complaint was occasional with slight dry cough. For a time, the patient was observed in a sanatorium.

Physical examination of the lungs, six months after the accident, was negative. Radiographic examination showed evidence of pleural thickening in the left costophrenic sinus. There was marked fibrosis and accentuation of the vascular markings in the right base, and a few scattered shadows strongly suggesting a saccular type of bronchiectasis. There was some pleural thickening in the right interlobar fissure.

*Discussion*—The findings pointed to a chronic indurative fibrous process involving chiefly the right base and a saccular bronchiectasis in the same region. There was no evidence of tuberculosis.

In this case, disability followed the sudden lifting of a barrel and was associated with pain in the upper right chest. It is well known that strain of the character described may increase the pulmonary and pleural tension so as to produce tearing of a capillary, or more likely of some pleural adhesion. It must be assumed that this is what occurred in the case.

For the period of hemoptysis and for the period of rest in the sanatorium that followed, the disability may be partially attributed to the alleged accident. Six months after the accident, the patient showed no further symptoms or signs that could bear any causal or aggravating relationship to the original accident.

The changes that were shown in the lungs by x-ray examination six months later were of old standing. They had probably taken years to develop and

could, from their pathology, in no way be attributed to the strain of lifting.

Therefore an arbitrary period of disability had to be decided upon as an equitable consequence of the alleged accident.

Hemoptysis is only a symptom and in itself is no aggravating influence upon an existing pulmonary condition. This fact is not enough understood, particularly by the laity. The impressiveness of blood expectoration is so great to most people that they lay to it any subsequent aggravation of the underlying lung disease.

Hemoptysis is a common symptom also in chronic heart disease, particularly mitral stenosis, and its occurrence after strain does not indicate aggravation. Physical strain may cause rupture of a capillary in the congested lungs. But when that has subsided, the underlying disease remains *in statu quo*.

Therefore, it must be remembered that expectoration of blood is only a symptom, and does not usually initiate pathological changes in the lungs. It may cause disability insofar as treatment for hemoptysis usually consists of rest for a period of time. This time is generally employed to advantage in establishing a definite diagnosis.

The following case and, in a measure, the one that immediately precedes (Abraham G.) illustrate the importance of hemoptysis in the discussion of compensation claims.

Jacob S., an egg-candler, 45 years old, lifted a sixty pound case and expectorated some blood-streaked sputum that day and two days later, after occasional coughing. He had vague pain in the left submammary region and the back of the left chest, but

had no recurrent hemoptysis, no night sweats, and no loss of weight. He remained generally in good condition during a long period of observation.

Physical examination, including x-ray and sputum examination, were essentially negative except for fibroid changes at both bases and in the left second costal interspace.

*Discussion*—Giving the patient credit for a relationship between the alleged strain of lifting and the blood-streaking of his sputum, this case presents no consideration of any prolonged disability, nor of any aggravation of a previously-existing condition. The patient expectorated some blood a few days after this strain, which necessitated his remaining at home for several days, under medical observation. That is the entire picture of disability that may be attributed to the accident.

Otherwise, the patient presented no evidence or any disability whatever in his cardiovascular or pulmonary condition. The occasional crepitant râles heard in the left apex region suggested the existence of a very incipient pulmonary lesion from which the blood might have originated. There was no other clinical evidence to show activity of this lesion, and we cannot assume any aggravation due to the hemoptysis.

As we already stated, hemoptysis is only a symptom of a condition and does not in itself (if slight, as in this case) aggravate or precipitate any complications.

X-ray findings were entirely negative and two sputum examinations were equally negative. The heart condition was negative and the electrocardiogram was also negative.

We therefore expressed the conviction that the patient may be given the benefit of considering a causal relationship between the alleged strain of lifting and the subsequent expectoration of blood. Altogether, an arbitrary period of disability of three or four weeks would more than cover any consequences due to the alleged strain. The claimant was soon after the alleged accident able to resume his regular occupation.

After a long lapse of time following the first examination, the following new facts revealed themselves. Before the alleged accident, the claimant had some bronchial condition of uncertain diagnosis for which he was bronchoscoped. A pathological section was made into the mucous membrane of the bronchus on the left side, producing an open wound there. The alleged accident occurred two months later, with slight hemoptysis. The source of this can now be definitely localized to the bronchial wound, which was a vulnerable point in the lungs.

The above discussion therefore still stands fundamentally valid as to both the medical and compensation liability aspects in this case. We must therefore still assume the possibility of a relationship between the alleged strain of lifting and the blood streaking of the sputum that followed immediately after. However, the hemoptysis was of short duration, not abundant, and in itself did not produce disability. As soon as the first signs of blood-streaking subsided, the relationship to the alleged strain ceased.

*Pre-Existing Heart Disease*—Pre-existing heart disease is often discov-

eried at the time complaint is made of symptoms developing during work Cases of this kind form a very large group in which the amount of liability is extremely difficult to estimate The relationship between the accident and the symptoms must remain speculative since often we do not know exactly what pathological changes were induced by sudden strenuous effort, or by direct injury In these cases, the question of aggravation of a previously existent heart condition must be considered Even without the history of accident, the patient's symptoms can often be fully accounted for by his previously existing disease And these symptoms would eventually have developed without any accident

Charles L., a young chauffeur aged 19, while lifting a package of 150 lb, felt sharp pain in the pit of the stomach which persisted After a few hours of driving his truck, he began to feel shortness of breath and fatigue and frequent rapid paroxysmal palpitation with a sensation of fulness in the neck and left hypochondrium and precordial pain

Physical examination two months later revealed the presence of long standing chronic rheumatic mitral stenosis and regurgitation and also chronic aortic regurgitation These findings were confirmed by polygraphic, electrocardiographic, and x-ray studies There was distinct precordial bulging Tonsillectomy had been done some years before, although tonsillar remnants were still present

*Discussion*—The evidence of long-standing heart disease was very marked in this case The patient had for years had chronic valvular rheumatic disease involving the mitral and aortic cusps for which, in all probability, tonsillectomy had been performed ten years before

If the patient's assertion is to be fully credited, pain developed immediately following the alleged exertion This, together with the other cardiac symptoms, would therefore be considered a temporary aggravation of his previously existing affection

An arbitrary period of a few months to a maximum of a year may be allowed for such aggravation to subside In this case, it appears to us that allowance of an arbitrary period of four months' disability is entirely equitable Certainly, there was no evidence of any permanent organic alteration produced by the alleged accident

Peter S., a stock clerk 59 years old, while supporting a crate weighing 800 lb on the end of a truck, felt a sensation of discomfort and momentary sharp sticking pain in the precordial region He continued his work, paying no further attention to this occurrence That night, while walking home, he felt an unaccountable shortness of breath and a choking sensation He felt dizzy and weak and had to sit down for rest He continued his work for a week, despite these symptoms which continued and recurred on exertion A week later, he took to his bed for the increased dyspnea and precordial pain The patient resumed sedentary work, but found walking difficult on account of shortness of breath and occasional precordial discomfort

The clinical examination and the special studies made in this case gave indisputable evidence of the existence of advanced arteriosclerosis with hypertension and myocardial disease The blood pressure was 210/104 These findings were supplemented by the x-ray observation of an enlarged heart with dilatation and sclerosis of the aortic arch, pulsus alternans in the polygraphic tracings, and the abnormality of the *QRS* and *T* waves in the electrocardiogram, showing intra-ventricular block

*Discussion*—This entire picture existed before the accident as it was the

result of a long-standing and gradual process. The accident alleged comes into consideration in this condition only in having produced a momentary sensation of discomfort and sharp pain when the patient exerted himself in supporting a heavy crate. It is conceivable that this physical strain produced a natural increase in aortic pressure, super-imposing upon the previous pathological process a mechanical factor in the further distension of the aorta.

Characteristically, such an occurrence produces severe pain, usually of long duration, associated with immediate cardiovascular symptoms and relatively marked disability. In this case, the claimant resumed his work for perhaps two hours, avoiding the more strenuous efforts. The real symptoms which eventually produced the disability came on a few hours after the accident, while walking home that evening. At that time, he felt dyspnea, fluttering in the chest, dizziness, weakness, etc. His attempts at work after the accident aggravated his symptoms so that he found it necessary to avoid all exertion for a time.

Judging from the physical and special findings in this case, an eventual disability was not far distant. A period of perhaps six months under the best conditions of care might be allowed as an arbitrary period, after which the patient's disability would have occurred spontaneously. We may therefore conclude that the alleged accident in this case precipitated the disability to the extent of this length of time.

Antonio A., a longshoreman aged 47, had been working at his occupation without

previous disability for twenty-seven years. Then one day, while unloading a ship, a heavy bale fell down on a hand truck. The handle of the truck struck the patient in the front of the left chest and knocked him down unconscious for five minutes. After a week in bed, he developed a burning sensation in the upper sternal region and sticking precordial pain. He felt sudden faintness with palpitation on walking and weakness which increased with exertion.

Physical examination 20 months after the accident showed enlargement of the heart. Over the aortic area, there was heard a loud, rough, blowing systolic and diastolic murmur transmitted to the vessels of the neck and down along the sternum. There was other evidence of aortic regurgitation, including water-hammer character of pulse and low diastolic blood pressure. Radiographic examination showed marked accentuation of the left ventricular curve and diffuse dilatation and sclerosis of the aortic arch. The Wassermann test of the blood showed a strongly positive (+++++) reaction.

*Discussion*—This patient suffered from aortic regurgitation and aortitis of the suprasigmoid portion of the aorta. The strongly positive Wassermann reaction indicated that syphilis was a causal factor in the production of the heart condition. The injury that the patient sustained, severe enough to have caused unconsciousness, may have contributed to aggravate the condition, causing the subsequent disability. According to the history that we obtained, the symptoms of disability ensued promptly after the accident. The disability in these cases is usually prolonged, the pain persisting and the symptoms often progressing.

In this case, of course, from the present available data, no arbitrary period of disability can as yet be established. After a length of time and repeated examinations, however, it will

be found that the patient's ability to work returns. At that time, in retrospect, an arbitrary period can be recognized.

*Hyperthyroid Disease*—Thyroid disease may be found on examination some time after an alleged accident. The patient will often attribute his condition to the accident, although it may have, without his knowledge, pre-existed. In fact, this is the usual instance in such cases.

We find an underlying constitutional disposition, and the question to decide is the competency of the accident to precipitate hyperthyroid symptoms. It is well known that hyperthyroidism shows periods of spontaneous remissions or of aggravation. The intercurrent accident at any phase in these cycles must therefore be properly evaluated as an exciting factor.

Richard D. aged 26, a young fairly well-nourished plumber of nervous temperament, while lifting a sink weighing 250 lbs., suddenly felt rapid forceful palpitation. He had a feeling of exhaustion, nervousness, tremulousness throughout the body, tremor of the fingers and flushing of the face. He felt "winded", but continued at work for the day. After a day of rest, he returned to lighter work, but found even that produced palpitation, shortness of breath and mild localized precordial aching pain at times or an occasional attack of paroxysmal tachycardia.

Physical examination, two months later, showed considerable enlargement of the thyroid isthmus and both lobes. There was a suggestion of exophthalmos and fairly well-marked von Graefe sign. The heart action was rapid and regular, with a forceful impulse, systolic apical murmur and somewhat elevated systolic blood pressure. The basal metabolic rate was +33, indicating a definite increase over the normal metabolism, due to hyperthyroidism.

*Discussion*—In short, the patient presented the cardinal symptoms and signs of exophthalmic goitre. He dated his illness, however, from the time of the alleged accident, and claimed compensation on the assumption of its accidental origin.

We may grant the possibility that the alleged exertion did produce a functional effect which brought the symptoms to the patient's attention. These would have eventually appeared with the progress of his condition. He did not suffer from the characteristic symptoms of heart strain and in our opinion did not develop any organic changes as a result of his exertion. So that at most, we may assume a temporary aggravation to have taken place. We have, of course, excluded acute intra-thyroid hemorrhages as a possible cause of the hyperthyroidism.

We therefore believe, in this case, that an arbitrary period of three months of disability may be allowed for the functional disturbances precipitated by the alleged accident. The subsequent symptoms must then be referred to the underlying thyroid condition as a result of which he may remain disabled for a long time.

Ethel M., a waitress 21 years old, dates her hyperthyroid symptoms from the time of an electric burn of her hand that she sustained while at work. She remained unconscious for a few minutes, and for two weeks after the accident, her legs felt stiff and numb. The right thumb and index finger were burnt and discolored, but healed after a month's treatment. After the accident, the patient began to feel a choking sensation in the throat, and the thyroid region swelled. The patient was nervous, easily flushed, had a tremulous feeling in the chest, digital tremor, and lost moderately in weight.

Physical examination, one year after the accident showed the thyroid isthmus and both lobes diffusely enlarged, the presence of a slight von Graefe sign, mild tachycardia, and slight digital tremor. The basal metabolic rate was normal.

*Discussion*—It is well known that emotional stress contributes to the onset of, or aggravates a thyrotoxic condition. When, however, the accident is relatively mild and the thyroid condition almost a year later is also mild, such as was found in this case, one cannot reasonably attribute the hyperthyroidism to the alleged accident. In fact, causal relationship between the accident and the thyroid condition then becomes questionable. If we accept the details of the history and the long convalescence in bed from the slight burns of the fingers, we must assume some nervous shock to have taken place as a result of the accident. The symptoms may have had some element of origin in the alleged accident.

It may also be granted that the absolute disability, according to the history, lasted one or two months during which time the patient was confined at home under the care of her physician. The physical examination and study of the basal metabolic rate one year later showed only a very slight degree of hyperthyroidism. The symptoms were very mild and in no way disabling. The patient could resume her previous work without any difficulty.

The question still arises in such a case as to for how long a period the liability for compensation is impossible. In the present case, the patient suffered no disabling condition one year

after the alleged accident. We feel convinced that an arbitrary period of disability within the period of the year since the time of the accident should justly and fully compensate the patient for any effects that the electrical burn produced.

Francis J., a young truck driver, aged 22, fell from his overturning truck, injuring his right leg which had to be amputated below the knee after a week after infection. A month later, the bone stump was repaired under general anesthesia. Another month later, he was discharged quite well with no complaints or symptoms referable to the heart, lungs, gastro-intestinal, genito-urinary, or nervous symptoms.

Our physical examination five months after the accident was essentially negative, but for a moderate tachycardia of 96 per minute, moderate digital tremor, and a slight von Graefe ocular sign. The basal metabolic rate was  $+19$ , indicating slight hyperthyroidism.

*Discussion*—The question arises as to whether the slight hyperthyroidism may have been produced or aggravated by the accident. That is entirely problematic. It is reasonable to assume, in this case, that hyperthyroidism developed following the emotional stress attendant upon such an accident as the patient suffered, and more particularly following the amputation of his leg.

As the patient's general condition was, however, good, it seemed to us that with only moderate care and with satisfactory nervous and mental control, he should improve and recover from this condition without any further consequences within a variable period of time. An arbitrary period of disability would therefore have to be determined at a later date, after re-examination of the patient.

*Thrombo-angitis Obliterans*—It is well known that the progress of thrombo-angitis obliterans is gradual and its onset insidious. It consists of a progressive obliterative affection of the arteries and veins of the extremities occurring spontaneously. When the affected part is elevated it becomes very pale, and when it is lowered it becomes slowly congested, but in all instances, the peripheral circulation in these regions is very poor. Trophic changes, and finally gangrene, take place necessitating amputation. The condition is most commonly slowly progressive, often with periods in which the condition remains stationary for a long time, and it may even become compensated by intra-vascular canalization, or even healed.

As a result of direct injury to an extremity, intravascular damage may ensue, or periarteritis with hematoma and compression of the vessel from without. In either case, obliteration of its lumen may result with distal gangrene sometimes requiring amputation. In normal individuals an adequate amount of trauma will be necessary to produce this result and the condition remains non-progressive after the immediate sequelae have been dealt with.

In cases of thrombo-angitis obliterans, we must assume that there is a greater vulnerability of the vessels and tissues of the extremities. Therefore, in cases in which the amount of trauma was slight, we must recognize the greater susceptibility of the injured parts. Secondly, the underlying disease persists and may progress even after the subsidence of the more direct effects of the injury. It is of primary

importance, therefore, to determine how much of this progress of the underlying disease should be attributed to the accidental injury.

The following scientific beliefs may be laid down as the basic factors in determining the exact amount of aggravation by trauma in any particular case.

1 An injury cannot be assumed to be the cause of the condition of thrombo-angitis obliterans (Buerger's disease) or of endarteritis obliterans (Wimwarter).

2 As an aggravating cause, it can only be of influence on the local involvement of the particular region injured.

3 It cannot aggravate the general process in the other extremities or elsewhere in the body, or at higher levels in the same extremity unless the phenomena following the injury point definitely to such aggravation.

4 If, after amputation, or after the local effects of the injury have subsided, the condition has remained stationary for a reasonable and acceptable length of time, the injury cannot be held liable for any subsequent developments. The acceptable, variable, though arbitrary, stationary period severs the injury and its effects from any relation to subsequent developments. It cannot be held that the injury may produce the unrelated and distant symptoms of the disease which may become manifest a long time after.

Harry B., a powerfully built man of 42, developed gangrene of the big and little toes of his right foot, a few days after a seven-pound iron fell upon it, across his shoe. These toes were amputated two months

later The middle three toes remained normal However, there was persistent pain in the stump scars and edema of the ankles after walking

The patient was a Russian Jew and had been an inveterate and heavy smoker of tobacco Physical examination, three weeks after the amputation, showed the existence of thromboangitis obliterans No pulsation was palpable in the dorsalis pedis and posterior tibial arteries of either foot There was deficient superficial circulation in both feet After two years of treatment, the condition was found to be not preceptibly progressive, having remained unchanged for a year

*Discussion*—From the history and the sequence of events in this case, we came to the conclusion that the cause of the gangrene was a traumatic thrombosis of the arcuate artery on the dorsum of the right foot This resulted in partial obliteration at the locus of injury with complete closure of the terminal vessels to the big and little toes There was a predisposing underlying thrombo-angitis obliterans

Certain of the etiologic factors that are usually associated with the development of thrombo-angitis obliterans were present in the above case The patient was a Jew of Russian antecedents who had smoked considerably and developed his condition within the usual period of incidence of this disease

The injury produced a local aggravation of the pre-existing endarteritis with gangrene of two toes There was no evidence, after a long period of observation, of any progress of the condition after the amputation of the toes The circulation of the foot remained unchanged There was no evidence of ascending involvement in the limbs which might be attributed to the acci-

dent Incidentally, the process in the other limbs which was also present and was present at the time of the injury could not have been affected by it

On the basis of the general principles above discussed, we believe that this case had reached a stage beyond the compensation limits for his injury, except for the loss of his two toes which remains a permanent defect

*Miscellaneous Progressive Conditions*—The same general principles apply to other long-standing conditions during which an industrial accident may occur and produce aggravating symptoms

The following two cases of chronic disease illustrate the application of principles of arbitrary period of disability in settling compensation claims following intercurrent accident

Sam S aged 68, fell to the floor striking the front of his chest for which adhesive plaster strapping was applied Two months later, he developed cough and expectoration and wheezing in the chest, with weakness, dyspnea on exertion, and some pain in the right lower thorax when he lifted a heavy weight

Physical examination, eleven months after the accident, showed a marked chronic emphysema and bronchitis that long antedated the accident X-ray of the lungs showed fibroid changes with calcification in both apices There were indications of pleural thickening, slightly more marked on the right side

*Discussion*—There was evidence in this case of thickening of the pleura on the right side There was, of course, abundant cause for this in the old extensive chronic bronchitis with pulmonary consolidation at the apices and chronic emphysema These conditions had existed for years Thick-



ening of the pleura is not a disabling condition. On the contrary, it is a healing process. At the time of the examination, the patient's respiratory symptoms of chronic bronchitis, wheezing in the chest, and some dyspnea were due to his old-standing condition and not to any pleural affection in the right chest.

However, the thickening of the pleura on the right side may have suffered some aggravation from the injury that the patient alleged to have occurred. We therefore believed that the compensation for the condition of the chest may arbitrarily be concluded within a period of a month, without the prospect of any further developments due to the accident.

Robert McK., a painter 34 years old, was holding a can of 50 pounds supported on his right shoulder, carrying it up a ladder. The weight swung him from the ladder, but by dint of his left hand-hold, he avoided falling. In twisting himself back to the ladder, he heard a "crack" in the right pectoral region with pain which radiated above the right shoulder. He continued work though the pain was slightly aggravated and prevented him from sleeping that night. After two weeks of rest, the pain gradually subsided.

Roentgenographic examination at that time showed irregular shadow localized near the base of the right lung, reaching out from the hilus region. But the peripheral portion of the right base was clear and the diaphragm was freely movable. Considered together with a four plus Wassermann reaction in the blood, the diagnosis was made of lues of the lung—probably an organizing gummatous exudate.

*Discussion*—It is hard to see how the luetic condition in the lung in this case can be a result of the unusual twisting of the chest. However, from the symptoms of the sudden sensation

of pain above the right shoulder with the occurrence of the accident, we must predicate the involvement of the lower pleural lesion. It is possible that a pleural adhesion existing there was torn away by the torsion. This is the most probable explanation which unifies the clinical picture in this case.

We may therefore say that the effect of the accident was transitory and the symptoms from it limited in duration. We should allow another month in the arbitrary period of disability for the duration of aggravation. The visible x-ray shadow may or may not have been initiated by the accident. It was probably an old process, and the adhesion that was hypothetically torn by the strain may have been part of this process.

4 *In Slow Healing Injuries of the Viscera*—Healing processes in the injured viscera are generally slow and, by virtue of their position, cannot be observed accurately. The physical signs are no adequate indication of the progress, and the evidence of the x-ray, though important, is not complete. We must therefore depend, in a measure, upon the symptoms and discoverable signs as the sole basis for our opinion as to the patient's disability.

In the following case, the persistence of hemoptysis is an obvious and undeniable indication that the process in the lung has not entirely healed, following direct injury to the chest. But even without the hemoptysis and without further complaints on the part of the patient, we must allow an arbitrary period of disability for the healing process to have become completed, after the bleeding stopped.

The details of this case are as follows

Paul R., a longshoreman 37 years old, was thrown twelve feet into the hold of a ship, fracturing three ribs. He has profuse expectoration of blood. He was treated by immobilization of the chest. Four months later, he still had slight cough and pain in the left chest in the region of the injury, and he continued to expectorate small amounts of blood clots after coughing.

Although the physical findings in the lungs were entirely negative, the occasional hemoptysis of which the patient complained must undoubtedly be attributed to the accident and the consequently injured lung tissue.

*Discussion*—In this case, the persistence of symptomatic evidence, particularly hemoptysis, precludes any anticipatory decision as to how long will be the period of disability. However, when finally the hemoptysis subsides, an additional arbitrary period of disability must be allowed for complete healing of the lung tissue and for recuperation before the patient is declared able to work.

5 *In the Mulder Post-Traumatic Hysterias*—The determination of an arbitrary period of disability in these cases often has a salutary effect upon the mental attitude of the patient. The finality of such a mode of disposition sometimes cures the patient spectacularly, as occurs in the summary settlement of cases of post-traumatic neurosis.

In the following case, a claim was made on the assumption of permanent disability produced by fright. This, however, was dismissed and an equitable settlement was obtained by establishing an arbitrary period of disability.

Rella G., a chambermaid 32 years old, was frightened by a police dog jumping at

her, his front paws on her shoulders, and barking at her. She had a headache that evening, but continued her regular work for three days, when she was released from work. A month later, she began to feel a choking sensation across her chest and slight shortness of breath on walking upstairs. She had a feeling of emptiness in the upper abdomen with anorexia. She also had sticking pains in the back and arms for a time. After a year, she still complained of occasional headaches and the vague symptoms narrated.

Careful physical examination and special examinations a year after the alleged accidental fright were entirely negative. The heart was normal in its mechanism, exercise tolerance, and all other tests. The reaction of the pupils, the peripheral vessels, and the activity of the thyroid gland were entirely negative. X-ray examination of the skull and lungs showed no organic changes. Other tests failed to indicate any disturbance in the anatomic (vagus) sympathetic or endocrine systems.

*Discussion*—In this case, careful discussion with the patient revealed the influence of problems of an economic and emotional nature. Certain domestic difficulties were found which, judging from the time of the patient's complaints, were coincident or soon followed the accident. Inasmuch as no organic changes were found, and as a certain amount of disability might, in fairness, be attributed to the fright, a short arbitrary period of disability was decided upon as an equitable settlement of the claim.

#### SUMMARY AND CONCLUSIONS

- 1 The gradation between total and partial disability and between partial disability and full capacity to work is almost always slow.
- 2 In determining the liability in a large number of cases, it is of

great assistance to apply the principle that may be called "an arbitrary period of disability" This must embrace the probable duration of all effects of the alleged accident, particularly in retrospect

- 3 Representative types of cases are given to illustrate the application of this mode of settlement
- 4 The largest number of these cases

comprises underlying progressive disease where the accident produced temporary aggravation

- 5 Particular discussion is given to pre-existing pulmonary tuberculosis, chronic heart disease, thrombo-angitis obliterans, and hyperthyroidism
- 6 This mode of settlement is advocated as equitable in the types of cases classified above

# The Spastic Colon\*

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**S**PASTIC colon is a functional disturbance of the colon, characterized by hypertonicity or spasticity of the colon, clinically by a variety of symptoms including abdominal consciousness, abdominal pain, constipation, flatulence, and a tendency toward introspection, while inflammatory changes may or may not be present

The term spastic colitis has sometimes been applied to this entity, but objection has been raised to employing a term that signifies an inflammatory state, since the condition is primarily a disturbance in function, while the inflammatory reaction may occur in the course of the disease

The essential mechanism of spastic colon is the hypertonicity. Several theories have been advanced to explain the causation of the hypertonicity. An unstable nervous system has been mentioned, a submerged fear complex acquired in early life has been held responsible, also an inherited spasmophilic tendency has been suggested. The direct etiologic factor is an open problem today, nevertheless it has been observed that usually the patient with spastic colon is a neurotic individual given to introspection, and that the

hypertonicity of the colon is a local manifestation of a general spasmophilic tendency

Since hypertonicity is the essential factor in the production of the symptomatology of spastic colon, an understanding of the factors that produce, or might produce it, become an essential preliminary to the rational treatment of the condition

Hypertonicity of the colon results when the normal rhythm of the intestine becomes disturbed and the contraction waves are accentuated. The tissues involved in the mechanism of hypertonicity are the muscular layers of the colon and their innervations

It is a truism in medicine that the bowels move by virtue of being bowels. This view is consistent with the broader view of biology that involuntary muscle fiber possesses the intrinsic property of rhythmical activity. The correctness of this view with reference to the intestine was first shown by the experimental studies of Bayliss and Starling who in 1899 showed by means of the enterograph, that when the gut is stimulated at a point, there results a contraction above the point of stimulation and relaxation below it. This wave of contraction passes down the intestine caudalward. This phenomenon takes place when all

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the nerves to the intestine from the central nervous system have been cut, hence this coordinated peristaltic wave is caused by a mechanism that exists within the intestine itself. This mechanism has been shown to be a peripheral nervous system lying within the wall of the intestine for the purpose of bringing about the necessary coordinated movements for the propulsion of the intestinal contents. This nervous system within the wall of the intestine is spoken of as a vegetative system in contradistinction to the sensor-motor system of the central nervous system.

The cells which cause the contraction waves are the nerve cells of the plexus of Auerbach. The presence of receptor nerves for this myenteric reflex has not been definitely established, but Ranson states that most physiologists assume the existence of sensory fibers in the gastrointestinal mucosa.

Hence in the consideration of the hypertonus of the colon, we bear in mind that there exists a vegetative nervous system within the wall of the intestine capable of causing contractions of the intestine, and that this system commonly receives its stimuli from the intestinal contents. Hence by inference it is assumed that hypertonicity may be initiated by material within the lumen of the intestine.

The intestine, however, has other nerve connections besides the vegetative system within its own walls. It receives connector fibers from the pelvic nerve which arises from the first, second and third sacral roots, and from the sympathetic branches of the superior mesenteric ganglion, the inferior mesenteric ganglion, and the

pelvic ganglion, and through these the colon is placed in relayed contact with practically every part of the body including the psychic processes and the emotions. Indeed it is a common observation, that the emotions have a direct influence on the functions of the gastro-intestinal tract, although some persons react more readily than others, that is, in some persons the functions of the gastro-intestinal tract are more susceptible to influence by the emotions than in others.

That there exists a psychic tonus of the alimentary tract is generally accepted by physiologists. In 1911, Cannon discussed the existence of this psychic tonus of the intestinal tract. The literature contains numerous experimental studies in both man and animals supporting this view. Alvarez describes an instance where a tracing was being made of the intestinal movements of a man who had a fistula in the first portion of the duodenum. During the course of the record taking, there was a sudden increase in the tonus of the patient with a corresponding increase in the amplitude of the rhythmic contractions without any apparent cause for the sudden change from the previous rhythm. Directly the observer heard the steam table come rumbling down the hall bringing the patient's luncheon. The patient was hungry and had heard it first. In this instance, impressions coming in through the auditory and possibly the olfactory pathways had caused an accentuation of the tonus of the intestine. This is a concrete instance of the so-called psychic tonus.

Lebensohn has shown experimentally that "reflexes occur from the eye to

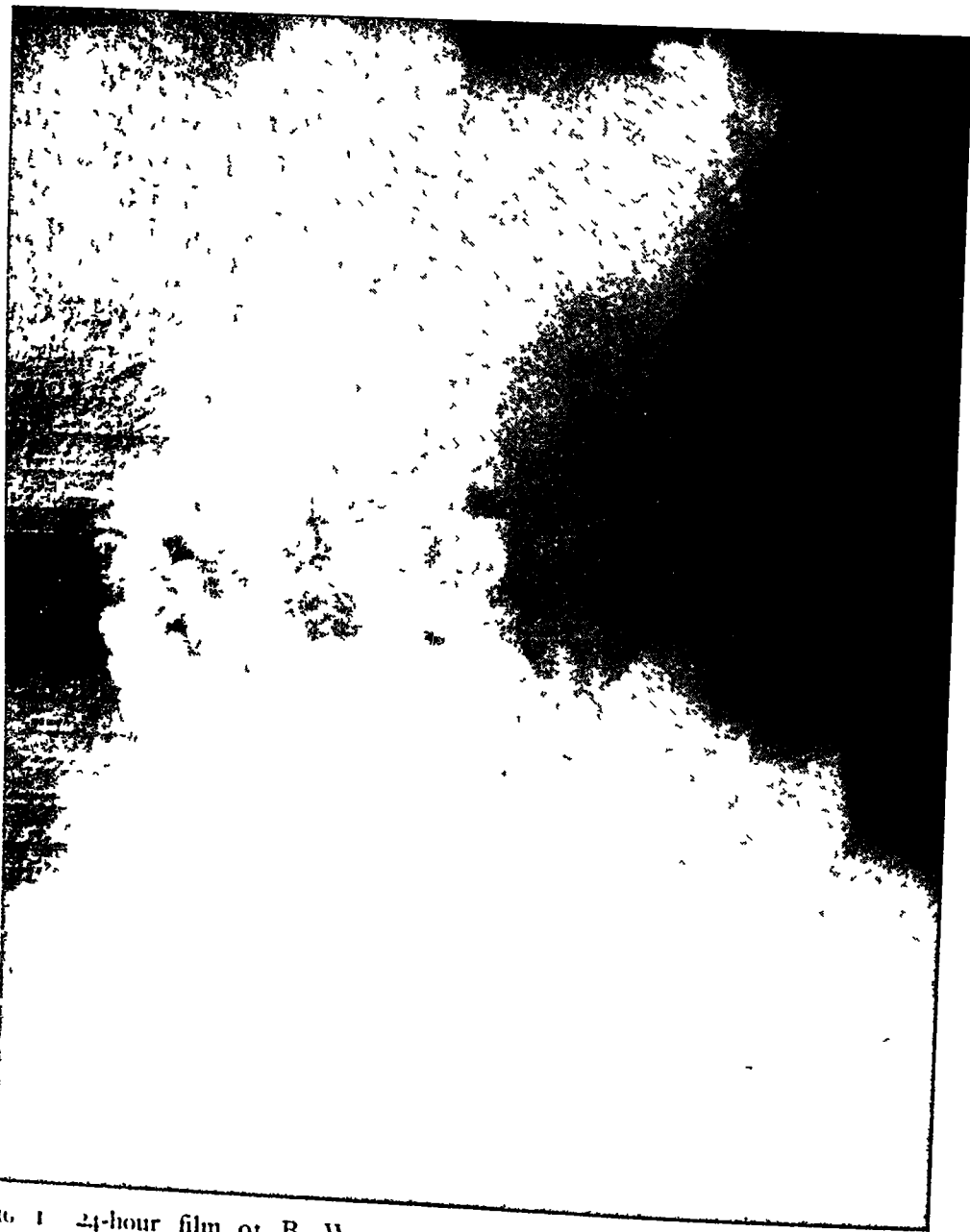


Fig. 1 24-hour film of B W, age 32, showing marked spasticity of descending  
limb

the stomach, and from the stomach to the eye

Using a stomach balloon connected with a water anemometer, tracings were made to demonstrate the effect of gastric motility of astigmatic errors and muscular imbalances artificially produced by wearing of cylinders and prisms, respectively. Errors of refraction or of muscular balance were definitely shown to exert a repressive effect on the motor functions of the stomach, while upon removal of such asthenopic irritants there was a release from inhibition."

Since there exists a psychic tonus of the gastro-intestinal tract, then by inference the psychic processes can produce a hypertonus of the gastro-intestinal tract. Hypertonus of the colon, then, can not only be produced by material within the lumen of the gut, but it can be produced by reactions elsewhere in the body including the emotions.

Dawson expresses the opinion that modern life makes trying and exacting demands upon the digestive system, and that there is a group of persons whose abdomens are overly sensitive to nerve impressions, and that in these people such reactions as fatigue, fear, anxiety, intensive application in any direction manifests itself in their hollow viscera. In some of them, the stomach may become irritable and hypertonic and may secrete an excess of acid, such patients develop the symptoms of gastric irritation. In others, the distal colon becomes irritable and hypertonic with a disturbance of its functions and they develop the symptoms of spastic colon. These patients are sometimes said to have "barometric abdomens," that is, their abdo-

mens indicate the state of their emotional reactions. Oddly enough, the male "barometric abdomen" commonly reacts by the gastric irritation syndrome, while the female "barometric abdomen" reacts by the spastic colon syndrome.

Among the predisposing causes, sex then seems to have a significant influence. Spastic colon occurs three times as frequently in females as in males. Other predisposing factors are the chronic cathartic or enema habit, irregular habits of living especially that of ignoring the defecation reflex, faulty diet, fatigue, insufficient exercise, faulty environment, emotional strain, etc.

The commonest symptom is that of chronic constipation. The stools are unsatisfactory to the patient, they are infrequent, difficult to evacuate, small in caliber, sometimes flat in contour or resemble sheep-dung stools. Many patients give a history of employing cathartics, stating that they are unable to have a normal bowel function. At first they may have taken an occasional cathartic because of the failure of the bowels to function properly, then the frequency of the cathartic or enema was increased until it became a daily occurrence, and finally even the daily cathartic fails to cause satisfactory evacuations.

Abdominal consciousness is another common symptom in the patient with spastic colon. The healthy person gives little thought to his abdomen, except on occasions such as when he is hungry, and hunger pains attract his attention to his abdomen, occasionally other incidents as perhaps a distended bladder or colon may attract his atten-

tion, but in general, he gives little attention to his abdomen. The individual with spastic colon is abnormally conscious. His abdomen holds an important place in his daily thought-life. He is introspective and analytic of his abdominal symptoms, and in time his entire interest may center in his abdomen, and his world of interest lies within his bowels.

Abdominal distress and pain are quite likely to occur where there is already a centering of interest in the abdomen. All degrees of pain may occur, from an intensification of the abdominal consciousness to acute paroxysmal distress. Sometimes the distress may be present as a dull ache. It may be general or localized. Localized pain is probably caused by the area of spasm. This symptom commonly gives rise to error in diagnosis, since localized pain may be confused with pain coming from contiguous organs as the appendix and gall bladder.

Epigastric distress is sometimes encountered and occurs at variable periods after eating. Sometimes it will simulate the gastric ulcer pain, however, as a rule it is not difficult to differentiate them. Whereas the pain of peptic ulcer is sharply localized to a small circumscribed area commonly referred to as a "finger point" area, and it occurs in a definite place in the food cycle, the epigastric distress of spastic colon is distributed over a much wider area and may extend the entire zone between the costal margins and is variable in its appearance, it may occur after some meals but not after others, after some foods but not after others and on some days and not on others. The epigastric distress

of spastic colon is not definitely periodic.

Many patients with spastic colon have had their appendices removed, after which they may feel better for a variable period of time when they have a recurrence of their symptoms. Eggleston states that in his series, twenty-two per cent of the patients had been subjected to appendectomy with little or no improvement, while five per cent had been subjected to cholecystectomy with no improvement, while Jordon and Kiefer report that twenty-three per cent of their patients with "irritable colon" had been subjected to appendectomy, and Bridges states that twenty-three per cent of his series of patients with chronic mucous colitis had been subjected to appendectomy with no demonstrable relief. There are undoubtedly instances where a differential diagnosis between appendicitis and disorders of the colon are difficult and a laparotomy may be justified, but Bettman strongly objects to appendectomy being performed on patients where the diagnosis is based on nothing more than "a history of indigestion and a poke in the right iliac region." Where a patient gives a history of a recurrence of the symptoms that were the indications for the appendectomy, disorders of the colon are to be considered including spastic colon. Elsewhere we have called attention to the frequency of appendectomy in patients with redundant colon.

Mucus in the stools is of frequent occurrence. The amount will vary greatly with the patient. There may be a few bits of mucus attached to the stool, or large quantities of mucus shreds or casts. Where the amount of





FIG 2 24-hour film of K M, age 38, showing marked spasticity of distal half of the transverse and of the descending colon

mucus is large, the condition is commonly spoken of as mucous colitis. There is a growing tendency to regard spastic colon and mucous colitis as the same clinical syndrome. Mucous colitis is regarded as an advanced form of spastic colon. Eggleston states that "I sometimes find it difficult to differentiate between mucous colitis and spastic colitis except by the amount of mucus observed in the examination of the stool. It is true that the patient suffering from mucous colitis frequently passes nothing but mucus, often in the form of molds or casts, usually following an attack of rather severe abdominal pain, but I would conclude that these are the more severe cases of spastic colitis and that the only difference between them is in the severity of the symptoms." Further relationship between spastic colon and mucous colitis is suggested by the similarity of their etiologic factors, since in both there is probably a disturbance in the equilibrium of the sympathetic and parasympathetic control of the colon, especially of the distal portion.

Flatulence and gas distress are commonly present and are very annoying to the patient. This symptom is more likely to occur in the aggravated form of spastic colitis. It will be recalled that gases are normally liberated in the colon as the end product of digestion. These gases include carbon dioxide, hydrogen, nitrogen, methane, and to a lesser extent hydrogen sulphide. The absorbable gases such as carbon dioxide and to a lesser extent methane are absorbed into the circulation and excreted through the respired air, while the less absorbable gases as

nitrogen, hydrogen, and hydrogen sulphide are passed through the rectum. About one liter of gas is passed normally through the rectum daily, while larger amounts are absorbed into the blood and so eliminated from the intestinal tract. In normal metabolism a person is little distressed by the passage of gases, but when the formation of gas is excessive or its excretion impaired, the patient experiences abdominal consciousness and later abdominal distress. Spastic colon may interfere with the elimination of gas in three ways: 1, by its spasticity, it diminishes the lumen of the gut and so reduces the amount of available absorbing surface for the gases; 2, spastic colon is a common cause of constipation, and the retained fecal masses occupying space within the lumen of the gut further diminish the available surface for absorption; 3, the spastic colon is an irritable colon and occasionally an inflamed colon, and as such probably has a diminished capacity for the absorption of gases.

Other symptoms encountered are chronic fatigue, chronic indigestion, underweight, nausea, vomiting, introspection, insomnia, mental depression.

Upon physical examination, the patient as a rule is not acutely ill, but gives evidences of emotional tension, he is introspective and self-analytical. A slight degree of secondary anemia may be present, the general nutrition is slightly below par, the tongue is coated and the breath may be offensive, the blood pressure is usually low. The heart and lungs give no information of importance with reference to the disease. Examination of the abdomen shows tenderness over the

colon The pelvic colon is markedly spastic, ropelike, easily palpable and tender, the caecum, however, is seldom constricted and may be dilated, the transverse colon is the least tender part of the colon

X-ray examination reveals either a general spasticity of the entire colon or of segmented portions of it. Usually the distal colon is involved. In some instances the haustral markings are lost, and the colon may present a "shoe string" appearance. Delayed emptying time of the colon is common, also an incontinent iliocaecal valve may be present and the caecum may be dilated.

Examination of the stool will indicate a diminished caliber of the stools, and mucus may be present.

**Principles of treatment** In considering the principles of treatment of spastic colon, the following points come in for consideration

- 1 Spastic colon is a state of hypertonicity of the colon,

- 2 Spastic colon is a local manifestation of a highly irritable nervous system,

- 3 Hypertonicity of the colon can be initiated within the colon, or elsewhere in the body including the psychic processes,

- 4 The spastic colon is a constipated colon, and has acquired faulty habits,

- 5 The individual with spastic colon is usually a neurotic individual, and "the neurotic individual," says Jacobson, "has partly lost the natural habit or ability to relax",

- 6 The spastic colon is an irritable colon, and sometimes an inflamed colon

From the foregoing premises, the following principles of treatment seem rational

- 1 It is desirable to reduce the irritability of the colon,

- 2 Reduction of the irritability of the colon must be accompanied by a reduction of the general irritability of the central nervous system,

- 3 The colon having acquired faulty habits must be educated, or as the case may be, reeducated to function normally and periodically,

- 4 To accomplish these ends, the colon must be put into a state of rest or relaxation as far as it is physiologically possible to do so, and to accomplish this, the individual must be put into a state of rest or relaxation, after which the attempt is made to reeducate the colon to function normally

In the treatment of spastic colon, the following therapeutic agents are available

*Bed rest* The value of bed rest is well recognized as a general therapeutic agent and is supported by clinical experience. Bed rest helps to put the entire human organism into a state of relaxation. It reduces the total amount of sensori-motor functions as well as the psychic processes of the body. It reduces the nutritional needs of the patient from that of the ambulatory patient which is 2,500 calories to that of the bed patient which is 1,500 calories, and thus facilitates the problem of putting the colon into a state of rest by permitting a reduction of the work imposed upon the gastrointestinal tract.

*Diet* The control of the diet is an important factor in the management

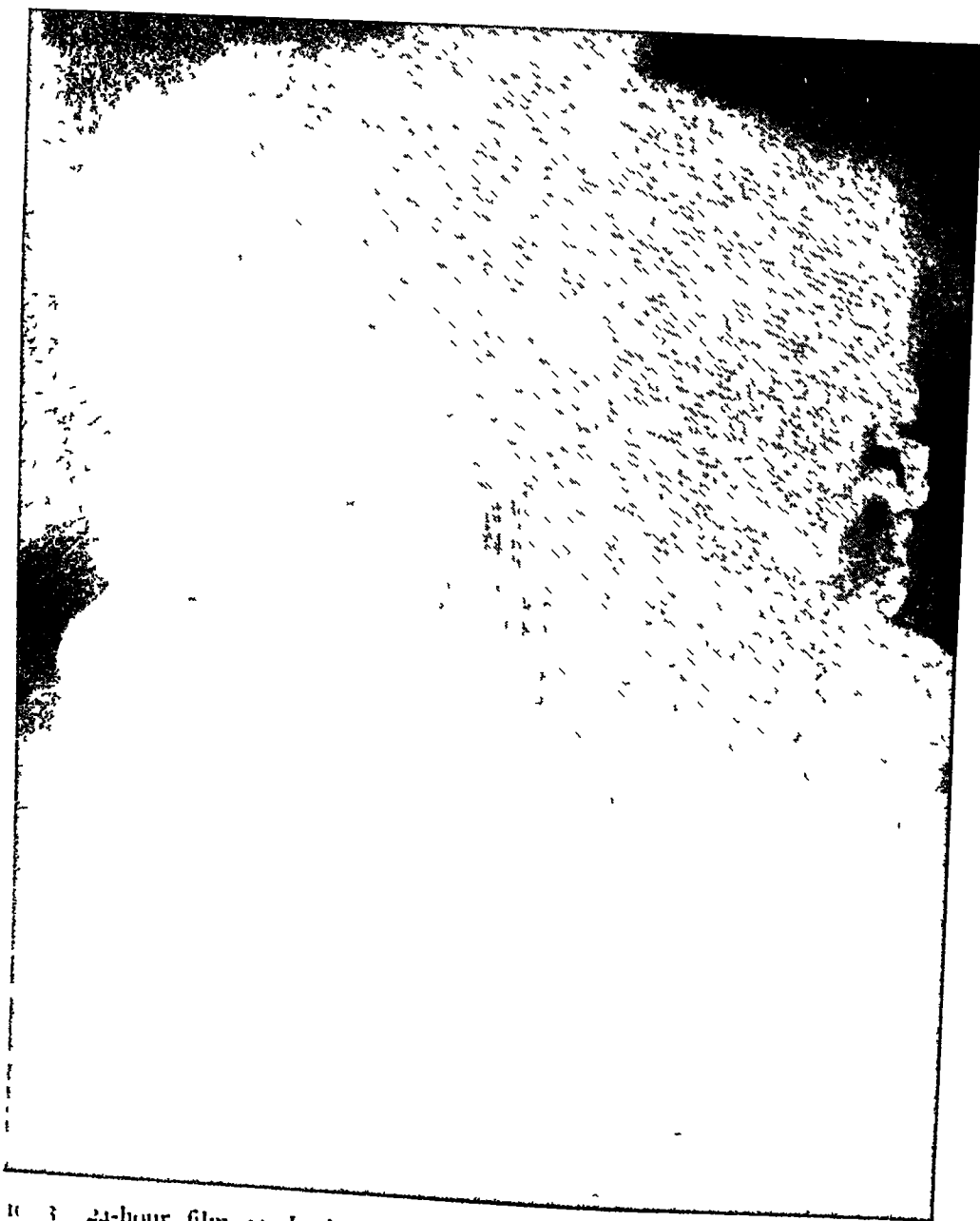


FIG. 3. 24-hour film of J. A. E., age 44, showing marked spasticity of the entire transverse and of the entire descending colon.

of spastic colon. Dietary indiscretions or an improperly balanced diet may have been a contributing factor in the causation of spastic colon, and once the hypertonus is initiated, ordinary food, or rather its end products can be the immediate stimulus for the maintenance of the hypertonicity. The first problem in the dietetic management is to put the colon into a state of rest. This is accomplished by the removal from the diet of all colon irritants. It will be recalled that the food elements which stimulate intestinal peristalsis are 1, roughage, 2, organic acids, 3, certain sugars. Foods which contain a high roughage content are bran, whole wheat, whole grain cereals, green vegetables as spinach, carrots, cabbage, asparagus, onions, tomatoes, parsnips, water cress, celery, turnips, beets, lettuce, legumes, as beans, peas, lentils, and nuts. Organic acids and sugars usually occur together in foods. They are found principally in the fruits as in figs, prunes, raisins, rhubarb, plums, grapes, apples, peaches, pears, raspberries, currants, strawberries, pineapple, orange. Lactic acid is a strong intestinal stimulant, and it occurs in certain foods without the presence of appreciable sugar as in buttermilk, sauer kraut, pickles and other fermented foods. These foods are removed from the diet and the patient is placed on a bland non-irritating diet made up to a caloric value of 1,500 calories and is chosen from those foods which contain little cellulose and a minimum of the organic acids. In this group of bland foods are the animal foods as milk, fish, eggs, the milk modifications as cheese, cocoa, chocolate, ice cream, the re-

finer cereals as white rice, farina, mashed potatoes, blanc manges, broths, custards, butter, etc. Such a diet is a residue-free diet and contains insufficient roughage for the normal individual. However in the first stage of the treatment it is desirable to give to the colon the maximum degree of physiologic rest. However in order to avoid a stasis within the colon which would follow from such a diet, the diet is supplemented by intestinal lubricants. These intestinal lubricants facilitate the movements of the colon without irritating it, from their nature they are soothing in character and have an emolient action on the colonic mucosa. Two methods of intestinal lubrication are available, both are employed. The first is to ingest mineral oil by mouth, the usual dosage is one ounce per day, the other is the use of the oil retention enema, commonly given as two to four ounces into the rectum upon retiring. The patient is instructed to retain it if possible, and can usually do so without difficulty or discomfort. The residue-free diet in connection with the intestinal lubrication is continued for about one week. The exact time is determined by the progress of the patient, although one week is about the average. A diet, however, like other forms of therapy, must contemplate the progress and ultimate recovery of the patient and must be adjusted accordingly, so in the second week, roughage is added to the diet, beginning with a few articles and gradually increasing them to the diet. At first the pureed cooked vegetables are added then the pureed cooked fruits then the plain cooked fruits and vegetables, finally the raw

fruits and vegetables. The following is the sequence of the foodstuffs thus added: first, pureed cooked spinach, carrots, spinach, beets, then the plain cooked celery, lettuce, squash, pumpkin, then the pureed cooked fruits are added as pureed apple sauce, prunes, pears, etc. In the third week, the uncooked fruits and vegetables are added cautiously, as orange juice, then the whole fresh fruits and vegetables. As long as the patient is in bed, the caloric values of the diet remains that of the basic maintenance diet or 1,500 calories. The patient is usually kept in bed for about two weeks, and in the third week is allowed to engage in moderate exercise and at this time the diet is increased to about 2,500 calories to allow for the additional expenditure of energy.

Medication has a useful and important place in the treatment of spastic colon. Two groups of drugs are employed, the anti-spasmodics and the sedatives. Of the antispasmodics, belladonna and its derivatives is the drug of choice. Belladonna is employed because it releases the intestinal spasm. It is given until its purpose is achieved. However, it is difficult to gauge accurately the effect of the belladonna upon the colon, so some of the other properties of belladonna are looked for as the index of its action. It will be recalled that when the pharmacologic action of belladonna is reached, the pupils begin to dilate and the throat becomes dry. These signs are then looked for, and belladonna is commonly given as eight drops of the tincture three times a day until the pharmacologic action of the drug is observed in dilated pupils

or the dryness of the throat, when it may be assumed that the drug has also acted on the intestinal musculature and released the spasm, after which the drug is discontinued or reduced in dosage. Patients exhibit marked variations in their response to belladonna, and the dosage is adjusted to their reactions.

A general sedative is commonly given in conjunction with the anti-spasmodic. Either the bromides or derivatives of barbituric acid as luminal are employed. The sedative is desirable because of the initial stimulating action of belladonna on the central nervous system, further it is desirable to depress all of the cerebral activities of the patient in the treatment of spastic colon in order to reduce the factors that produce the psychic tonus of the gastrointestinal tract. A simple procedure in the administration of both of these drugs is to give the usual dose of each of them until the patient complains of being drowsy or of inability to see clearly, when the drugs are then discontinued.

Local applications of heat to the abdomen have a soothing effect on the patient and help to divert his attention from his symptoms.

Foci of infection should be looked for, and if found, should be removed.

Usually in the third week of the treatment, the patient becomes ambulatory, and he is placed on a balanced diet which contains a moderate amount of roughage. He is instructed to take a moderate amount of exercise, and to continue the oil retention enemas at night. The belladonna may or may not be continued depending upon the reaction of the patient. The under-

lying neurosis may subside with the establishment of an agreeable routine for the patient, or it may require the attention of the neurologist

The prognosis in spastic colon is always guarded. Due to the underlying neurosis, recurrences are apt to occur

## SUMMARY

1 Spastic colon is a functional disturbance of the colon

2 The etiology is thought to be an underlying instability of the nervous system

3 It occurs commonly in women of the so-called "neurotic" type

4 The essential mechanism of spastic colon is the hypertonicity

5 Hypertonicity of the colon may be initiated locally by impulses originating in material lying within the lumen of the colon, or by impulses originating in other parts of the body

including the psychic processes, when the impulses are thought to be relayed to the colon through the sympathetic nervous system

6 The common symptoms of spastic colon are constipation, abdominal consciousness, abdominal pain, flatulence, and a tendency towards introspection

7 Neurotic individuals have partly lost the natural ability to relax

8 Treatment aims to reduce the irritability of the hypertonicity

9 The following therapeutic agents are available: bed rest, a bland non-irritating diet, intestinal lubrication, local anti-spasmodics especially atropine, general sedatives as bromides or the barbituric acid derivatives, local applications of hydrotherapy or physiotherapy to the abdomen, psychotherapy

10 The prognosis is guarded

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# The Intravenous Use of Epinephrine in Severe Bronchial Asthma

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THE following case report suggests that it is possible to secure complete relief in the severest possible type of bronchial asthma that apparently offers nothing but a prompt fatal outcome, by the use of epinephrine in small doses given intravenously, after the administration of the drug in large quantities hypodermatically in the ordinary manner and after morphia given to the danger point have completely failed. In this case, and in two others of mine of the same type, the procedure was a life saving measure, and it is trusted that its adoption elsewhere in similar cases will prevent protracted suffering and possibly further fatalities during otherwise uncontrollable asthmatic paroxysms, relieving the utter helplessness of other medical attendants in similar situations. The dosages used were two and three minims of the 1:1,000 dilution, repeated every thirty to forty-five minutes. The usual disagreeable epinephrine symptoms of pallor, tremor, headache, nausea and at times vomiting appear almost instantaneously with this method of administration of the drug, especially with the three minim dose but they are transitory, not severe, and were not objected to by my patients and there were no other ill effects. I know of no reports

in our medical literature advocating this line of treatment in what would otherwise be fatal asthma, hence this case report.

C E, age 29, civil engineer, first seen in December, 1930, gave a history of severe intractable bronchial asthma of several years' duration, during which time his daily epinephrine ration at times for weeks on a stretch varied from three to eight cubic centimeters. During not infrequent exacerbations morphia was required in one-half grain and three-fourths grain doses every few hours. No morphia was required or used except during the periods of extreme severity. He had been unconscious during two previous attacks. A double Caldwell-Luc operation gave complete relief to the asthma for four months, but for several months past, the asthma had been daily and at times severe. Intranasal examinations a few days previous to the onset of the attack to be described, by two independent nasal specialists, revealed no indications for further surgery or for local nasal treatment. Severe asthma began about noon, December 31, 1929. Epinephrine hypodermatically in one c.c. doses every two hours at first gave a measure of relief, such relief becoming of briefer and briefer duration, and finally of minimal degree, lasting only a few moments. From midnight to noon of January 1, 1930, fifteen and a half c.c. of epinephrine were used, including two doses of two c.c. each one hour apart. In addition, morphia, three-fourths of a grain, was given at six a.m. and one grain at eleven a.m., all without the slightest relief. About one p.m., the patient became comatose, remaining so several hours. The pupils were pin point, with



respirations of twelve to fifteen per minute and a pulse of one hundred and forty to one hundred and fifty that was scarcely perceptible. As three-fourths grain morphia doses were not unusual in this patient, and none of the drug had been used for several days past, and as the patient had been unconscious previously from asthma when morphia had not been used in any such dosages, it is doubtful that this was altogether morphia overdosage, coma not being unheard of in mild asthma of this type. In spite of this heroic therapy, the asthma continued constant in severity, without the slightest remission. From two p m to five p m strychnia and caffeine sodium benzoate were administered. At 5 20 p m, the patient was apparently moribund, sitting on the side of his bed held up by two attendants, totally unconscious, with extreme pallor, pulseless, unable to hold up his head, mouth wide open with saliva drooling—a most pitiful object—with the usual asthmatic respirations (fifteen per minute), easily audible in the adjoining room. Two minims of epinephrine were given intravenously without waiting for instrument sterilization. To the astonishment of all, there was some relief to the asthma and some general condition improvement. The following notes are taken from the nurse's chart:

6 00 p m	Epinephrine intravenously, 2 minims	No more improvement, but recovering consciousness
6 25 p m	Epinephrine intravenously, 2 minims	Brief nausea, conscious, some improvement
7 05 p m	Epinephrine intravenously, 3 minims	Brief nausea and headache. Vomited once, followed by immediate decided improvement
10 10 p m	Epinephrine intravenously, 3 minims	Immediate headache. Vomited once

This was followed in five minutes by such complete relief and relaxation that the patient was able to lie flat and sleep the balance of the night without further medication. Some five days later in a similar spell of almost equal severity, following the use of morphia, grain one-half, seven two to three minim intravenous dosages of epinephrine at similar intervals brought about the same complete relief after hypodermic administration had failed.

Since this last severe attack, by usual asthma treatment methods, it has been possible to hold this patient in comfort with from one to one and a half cubic centimeters of epinephrine hypodermatically in twenty-four hours, no morphia being required or used and same 6 weeks after the attacks above described, it was possible to omit epinephrine altogether.

From clinical observation, this patient seemed, among other factors, allergically speaking, hypersensitive to morphia in spite of his ability to use it in large doses. While this drug occasionally gave a certain amount of relief, and was usually used at the patient's request without the nausea and vomiting ordinarily seen in asthmatics sensitive to narcotics, such relief usually was only temporary, seemingly increasing the intractability of the subsequent asthma for many hours. His intradermal skin test to morphia gave a typical positive wheal and erythema, but this occurrence with morphia and other narcotics in the nonasthmatic is too com-

mon for this incident to be of clinical significance.

It is difficult to account for the failure of such large doses of epinephrine given hypodermically to give the slightest relief when such small doses are efficacious when given intravenously. It is hardly probable that constant repeated use of the drug in the upper

arms had altered the tissues so that absorption would not occur, as this point was taken into consideration and many of the doses used during this attack were given in the upper back and buttocks, never previously used for this purpose. It is more probable that with the enfeebled circulation accompanying the exhaustion of cases of this type, the rate of absorption of the epinephrine from the subcutaneous tissues into the blood stream is so slow

as to permit its partial or total oxidation so that its distinctive action is not possible. This is, of course, remedied by intravenous administration. It is almost superfluous to add that the routine intravenous employment of epinephrine in paroxysms of bronchial asthma is unnecessary and not recommended. The writer has had no experience with intravenous doses larger than three minims.

# Gastric Feeding As a New Treatment for Cardiospasm

By MOSIS EINHORN, M D, *New York*

I DELAYED the announcement of my new treatment of cardiospasm for the purpose of convincing myself of its beneficial results. During the past few years, I have treated a number of patients suffering with cardiospasm, and a follow-up of the cases revealed that there had been no recurrences. Recently, I have had occasion to treat a few additional patients, with the most satisfactory results, and I am consequently presenting the treatment to the medical profession, in order that they may apply same to their individual practice.

Although I have made an extensive survey of the literature on cardiospasm, up to the present writing, I have failed to find mention or suggestion of the principles outlined in my treatment. It is true, that reference has been made to gastric feeding, but only in extreme cases of cardiospasm, where food necessarily had to be forced through a tube, into the stomach, however, to my knowledge, gastric feeding as a treatment for cardiospasm has not heretofore been advanced.

I shall not discuss here the cause or mechanism of cardiospasm, as I am discussing this phase in a separate article,<sup>1</sup> but I shall merely present the

main principle involved in this treatment, namely, gastric feeding.

## *Gastric Feeding*

In gastric feeding, I use my new gastro-duodenal apparatus,<sup>2</sup> which consists of a special bucket and a marked tube (Fig 1). The main characteristics of the bucket are its three part composition, its capsule shape, spiral arrangement, and its lower part three times heavier than the upper part.

The tube is of semi-soft quality, which lessens the possibility of knotting or bending, a usual occurrence in a dilated esophagus. It is marked with a single black line, 20 inches from the bucket, and with a double black line, 27 inches from the bucket. At the end of the tube a rubber stop-cock is introduced.

This gastro-duodenal apparatus, with its special bucket, is superior to any of the others now in use, for the following reasons:

1 Swallowing of the bucket is accelerated, because of its capsular shape and weight, which is sufficient to permit the passage of the tube through the esophagus with a minimum of discomfort to the patient.

2 Because of its weight (11 grams), being heavier than any other bucket now in use, it maintains its in-

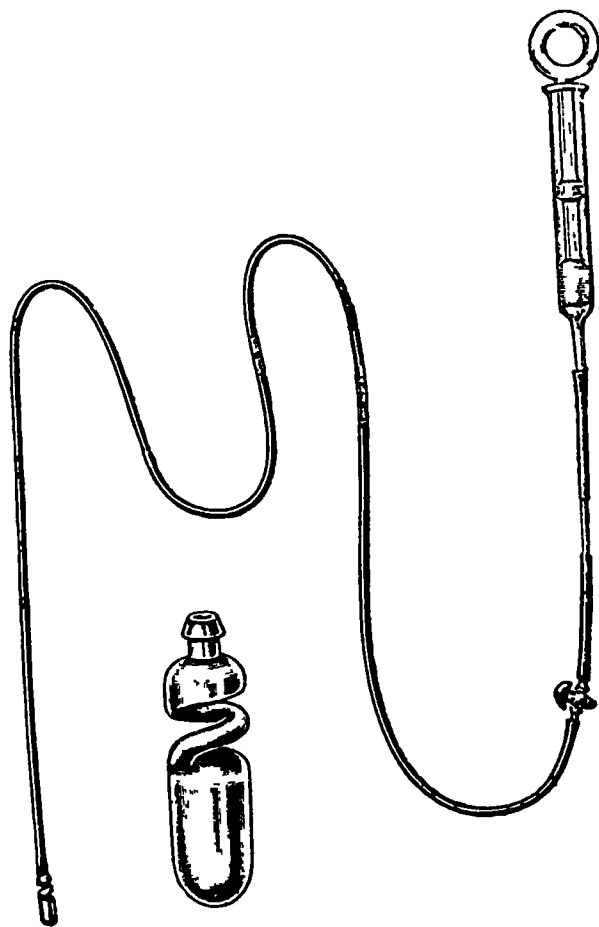


FIG 1

tended course along the esophagus, which is usually dilated in cases of cardiospasm

3 Its proper arrangement, the distal end made of solid metal, three times heavier than the upper part, causes the tube to be carried down to the lowest point of the esophagus in the region of the cardiospasm

4 Due to its weight, it overcomes the spasms at the cardia, and passes easily through the spasmodic area into the stomach

5 No silk cord guide is necessary as the bucket acts as a guide for the tube

#### *Method Employed*

The patient is placed in an upright position in bed or on a chair, and is instructed to open his mouth. The bucket, which is moistened and held between the thumb and forefinger, the middle finger being used as a base, is placed on the patient's tongue. He is then instructed to utter the sound Ah, and the tube is rapidly pushed into the esophagus. While concentrating on the act of swallowing, the bucket, due to its weight and capsular shape, is slowly carried through the esophagus into the stomach. The patient then continues to swallow the tube, until the first black mark, 20 inches from the bucket, is reached.

To ascertain whether or not the bucket has passed the spasmodic area and entered the stomach, the following test can be employed. Inject a small quantity of liquid through the tube with a syringe. The fact that the liquid can be withdrawn indicates that the bucket is still in the esophagus, above the spasmodic area but if the liquid cannot be withdrawn, the bucket has already entered the stomach. The patient is now instructed to swallow the tube midway between the first and second mark and a piece of adhesive tape is attached to the tube at this point.

After the tube has been correctly inserted feeding may be commenced. The patient is fed with the aid of the tube for a period of ten days. In order to insure complete rest and relaxation, it is preferable that the patient remain in bed throughout the course of the treatment. However, the treatment may also be ambulatory, if necessary.

Every three days, preferably in the morning, on an empty stomach, the tube is removed for cleansing purposes. At first, same is removed only a few inches, and the saliva which has accumulated in the esophagus, above the spasmodic area, is withdrawn with a syringe. The esophagus is then thoroughly washed, by injecting a solution of boric acid or luke warm water through the tube. When this process has been repeated several times, the tube is removed, cleansed with warm water, and reinserted into the stomach, in the manner previously explained.

This new treatment of cardiospasm, which I have outlined, is particularly beneficial in cases of cardiospasm, not

associated with any other organic gastrointestinal lesions. About ninety per cent of the group which I treated had simple cardiospasm, but no other abnormalities. Since, aside from this ailment, the cardiospasm patient is usually normal, he is able to partake of a variety of foods, providing these foods are prepared in liquid form, and can pass readily through the tube.

The feedings should be frequent, and in small quantities, not exceeding one and a half ( $1\frac{1}{2}$ ) glasses every two or three hours. Sharp and spicy foods should be avoided, also, extremes in heat or cold. Water may be taken through the tube, between meals, and thirst and dryness of the mouth satisfied with the aid of a mouth-wash.

#### *Diet*

Orange juice, grape juice, tea, cocoa, chocolate, coffee, milk, cream, mixture ( $\frac{3}{4}$  milk,  $\frac{1}{4}$  cream), tea and milk, egg-nog, farina, vegetable soup, celery soup, asparagus soup, chicken soup, barley soup, gruel, beef juice, spinach (liquid form), jello (dilute), custard, apple sauce, fruit sauce.

#### *Advantages*

- 1 Patient is free from the discomfort in the epigastric region which usually accompanies cardiospasm.

- 2 Complete rest is offered to the spasmodic area, including the lower part of the esophagus.

- 3 The intake of food can be increased with the aid of the tube, and weight incidentally gained.

- 4 The physical and psychic rest obtained by this treatment indirectly has a beneficial effect on the cardiospasm.

5 The constant presence of the tube at the site of the spasmodic area tends to counteract the spasms

6 Forcible dilation by special dilatory instruments is usually unnecessary

#### SUMMARY

Gastric feeding is advanced as a new principle in the treatment of cardiospasm. The apparatus used in this treatment consists of a special bucket, the lower part three times heavier than the upper parts. The treatment is usually given while the patient remains in bed, but, occasionally, may be am-

bulatory. The patient is fed through a tube, for a period of ten days, the diet including a variety of foods, in liquid form. The intake of food should be frequent, and in small quantities, not exceeding one and a half glasses every few hours. Sharp or spicy foods, as well as extreme hot or cold foods should be avoided.

<sup>1</sup>EINHORN, MOSES. New Conception of the Mechanism of Cardiospasm (to be published)

<sup>2</sup>EINHORN, MOSES. A New Tip for Gastro-duodenal Tubes, J A M A, 1926, Vol 86, pp 1615-1616

# Glycosuria and Recovery Following Methyl Salicylate Poisoning

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**A**CUTE intoxication with methyl salicylate is reported to have been fatal from a dose of one ounce. There have been recoveries following such doses and also deaths from smaller doses in children. The variable susceptibility to salicylic acid intoxication is likewise recognized. The following case is of interest because of the recovery following a large dose, and because of the discovery of glycosuria as a feature of the intoxication.

A nurse, thinking she was taking an ounce of saturated solution of magnesium sulfate, took the same amount of synthetic methyl salicylate instead. This was at 8 a.m. She explained the error as due to her practice of holding her nostrils shut when taking a saline. Chagrined at the mistake she said nothing at first, but later asked indirectly for advice in event of such an accident. She did not have the gastric lavage which an interne recommended. She felt well until five hours later when she vomited material which she said was oily and had a slight odor of methyl salicylate. Then vertigo and headache were noted. It was not until after fourteen hours that she sought medical care, with a "bursting headache," tinnitus aurae, almost com-

plete deafness, nausea, and vertigo, and partial delirium.

When magnesium sulfate and castor oil were administered they were promptly vomited. The vomitus apparently contained no methyl salicylate. Two stools voided during the hours preceding examination had shown no gross blood. Blood pressure, temperature, pulse and respiratory rates were not unusual. The repeated emesis of all fluids given by mouth continued for about 24 hours. Due to dehydration, urine was not secured until the morning following the taking of the poison. At this time the urine was found to contain much sugar, acetone, 0.1% albumin, but no casts. The blood sugar was 148 mg per 100 cc.

The patient felt well after five days. By the second day the glycosuria and ketonuria had disappeared, by the fifth day the albumin had vanished, and on the eighth day a sugar tolerance test was done. The original blood sugar level was 81 mg per 100 cc. The maximum, 195 mg, was reached an hour after ingestion of 50 g of dextrose. After three hours the blood sugar had dropped to 126 mg. The tolerance was evidently still a bit impaired. Two weeks later the same test

was made. The initial blood sugar value was 102 mg, the maximum of 125 mg was reached in one-half hour, and the return to 92 mg had been accomplished after two hours. Glycosuria did not accompany either test. Blood sugar determined before breakfast six months later was 78 mg per 100 cc. The urine at that time was free from sugar, acetone, and albumin. The nurse had been well and on regular duty throughout the interval.

It is evident that there was in this case a temporary and presumably perfectly recoverable injury to the kidneys and the carbohydrate metabolizing mechanism, as well as to the central nervous system. The renal and nervous system injury have been recognized in the cases already reported in the literature, which is cited by Pincus and Handley<sup>2</sup> and by Woodbury and Nicholls. Disturbance of carbohydrate metabolism has not re-

ceived attention. Ketosis has been mentioned by these authors but no significance was attached to it. Pincus and Handley<sup>2</sup> made detailed examination of the blood of one case, and found blood sugar 145 mg per 100 cc. This was taken at the onset of convulsions, following which elevation of the blood sugar is known to occur. The absence of other known reason for hyperglycemia, glycosuria, and a disturbance of sugar tolerance in this case leads us to suggest that these phenomena indicate direct toxic action of the methyl salicylate. The site of injury cannot be specified.

<sup>1</sup>PERERSON, F, HAINES, W S, and WEBSTER, R W. "Legal Medicine and Toxicology," 2nd Ed, Phil, 1923, v 2, p 717.

<sup>2</sup>PINCUS, J B, and HANDLEY, H E. Bull Johns Hop Hosp, v 41, p 163, 1927.

<sup>3</sup>WOODBURY, F V and NICHOLLS, A G. Can Med Ass'n J, v 18, p 169, 1928.



# Experience With the Colloidal Silver Treatment of Cancer\*

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AT the time of initiation of the lead treatment of cancer by Blair Bell it was claimed<sup>1</sup> that lead acted as a specific poison for undifferentiated tissues, whether embryonal or neoplastic. Colloidal lead was used in preference to ionic lead because of its lower toxicity, not because any beneficial action was anticipated from the colloid as such. Later work has shown that lead is deposited more freely in the liver, bones, spleen and kidneys than in the tumor,<sup>2</sup> that therapeutic doses do not necessarily induce abortion,<sup>3</sup> and that the highly embryonal chorionic epithelioma is not conspicuously lead sensitive.<sup>4</sup> The opinion has therefore repeatedly been expressed, and is summarized in the Report on the International Conference on Cancer, London, 1928, that the occasional beneficial effects observed after the treatment of cancer with colloidal lead are not due to any specific action of the lead on the tumor cells, but are due either to the action of lead as a general tissue poison or to the action of the colloid in producing some type of systemic shock.

The present work was based on the hypothesis that the action of colloidal

lead was due to its effect as a foreign colloid. If this were true, then other colloids might be found which would have the beneficial action of colloidal lead without the high toxicity which constitutes so serious an obstacle to its use. As silver is toxic only in massive or long-continued doses<sup>5,6</sup> the therapeutic effects of colloidal silver in the treatment of cancer seemed worthy of investigation.

Considerable experimental work on the effect of intravenous injections of silver colloids has been reported in the literature<sup>7,8,9</sup>. Most of the preparations used contained organic colloids as protecting agents, so that it is difficult or impossible to determine whether the constitutional effects observed were due to the silver or to the protecting colloid. Hence it was decided in the present work to use unprotected colloidal silver, both for the sake of securing clear-cut results, and in order to avoid the danger of shock. It was felt that these advantages would outweigh the disadvantages of using material as dilute as the unprotected colloid.

The method of the preparation of colloidal silver was essentially the same as for the preparation of colloidal lead.<sup>10</sup> It consisted of main-

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taining an arc between silver electrodes immersed in a suitable solution. The solution was protected from dust and from carbon dioxide, and was maintained at a temperature of 15°-35° C. by means of an ice bath. The solution used was dilute sodium carbonate (0.015 molar). This was chosen because it was non-toxic, and was an efficient stabilizing agent for colloidal silver. As arcing proceeded in this solution the concentration of colloidal silver rose to a maximum and then, upon further arcing, fell to zero. As the stability of the colloid was somewhat less when arcing was continued past the maximum of concentration, the arcing was discontinued just before the maximum was reached. The colloid was then centrifuged for five minutes with a force of 1000 x gravity, sampled for analysis, closed with rubber seals, and kept for use.

Colloidal silver so prepared contained about 0.30% silver, of which about one-tenth was ionic, and the remainder was colloidal. It was dark bluish-brown to black in color. It was stable for at least a year at room temperature. It was coagulable by boiling, and hence could not be sterilized by heat. For this reason preparations intended for clinical use were made up with sterile precautions. Tests on glucose broth and agar with 72 hours' incubation showed these sols to be sterile. They also had considerable bactericidal action on a virulent strain of *staphylococcus aureus*.

The preparation was tested by intravenous injection in three rabbits before being used for humans. Single injections up to 5 mg. silver per kilogram body weight were made. The

largest total amount of silver used was 22 mg. per kg. administered in eight injections over a period of 60 days. In no case was any reaction observed after an injection, none of the animals lost weight during the treatment, there was no significant change in hemoglobin or red cell count, significant rise in white cell count occurred after only one of seven injections when it was determined. In one animal the blood sugar was determined before and after four injections, and was not found to change significantly. Subcutaneous injections of  $\frac{1}{2}$ -1.0 cc of colloidal silver in the ears of these animals did not produce inflammation or necrosis, the silver remaining visible as a black deposit beneath the skin. Two of the animals were killed and examined postmortem. Gross and microscopic examination revealed no abnormalities beyond slight congestion of liver and spleen.

On the basis of this work on animals it was concluded that the toxicity of the colloidal silver used was low enough to warrant its employment in human subjects. The cases selected for this treatment were so far advanced that it was reasonable to conclude that no other form of therapy would be beneficial. In two cases the silver injections had been preceded by two cycles of x-ray treatment without any appreciable benefit.

Although the toxicity of the silver appeared to be much less than that of lead, it was necessary, however, to limit the amount injected because of the primary systemic reactions.

In this connection it would be well to note that Weil<sup>12</sup> in 1913, employed colloidal copper intravenously for the

treatment of cancer at the Memorial Hospital. The colloidal copper was given intravenously every day or every other day in doses up to 21 milligrams and total amounts up to 450 milligrams. The treatment was followed by slight fever, chills, nausea, loss of weight, and occasional albuminuria. In two instances, copper was found in the livers but not in the tumors. There was occasional subjective improvement but never a decrease in the size of the cancer.

### CASE REPORTS

*Case Report No 1 A V*, a married Cuban woman, aged 44, applied to the Memorial Hospital on Dec 19, 1928, complaining of a recurrent tumor of her right breast. The onset of menstruation was at 13½ years. Menses were normal until Oct 1928, when she began to have menorrhagia

of 15 days duration. She had one child, aged 26 years, this child nursed both breasts equally for one year.

Three years before application to this hospital, i.e., in 1925 she first noticed a lump in the upper portion of the right breast. In 1926, a mastectomy was done at another hospital. In April, 1928, she developed pleurisy with effusion on the right side, she had four pleurocenteses. In May, 1928, a recurrent tumor mass appeared in the scar of the previous operation. She has had considerable dyspnea.

She was in good general condition and weighed within two pounds of her maximal weight. Examination of the lungs showed a broad zone of dullness to flatness and decreased to absent breath sounds at the right base. The liver was not palpable. On the right anterior chest wall was a bulky, lobulated, fungating tumor, 10 centimeters wide. It was fixed to the chest wall. In the lateral portion of the scar was another nodule and in the chest wall below the scar and in the

#### Intravenous injections of colloidal silver solution

12-27-1928—27	milligrams of colloidal silver in 77 cc of solution
1- 2-1929—25.4	milligrams of colloidal silver in 82 cc of solution
2- 4-1929—32	milligrams of colloidal silver in 130 cc of solution
7-31-1929—16	milligrams of colloidal silver in 65 cc of solution

#### Laboratory Examinations —

Blood Counts	Hb	R B C	W B C	Ncut	Large L <sub>3m</sub>	Small L <sub>3m</sub>	Bas	Eos	Trans Cells	
12-27-1928	65	3,460,000	11,800	72	5	15	1	—	7	
1- 2-1929	65	3,400,000	12,200	71	4	20	—	3	2	Polychromato-
1-16-1929	65	3,510,000	9,300	76	7	14	—	—	3	philia
2- 4-1929	70	3,300,000	8,840	70	7	20	1	1	1	
2- 7-1929	70	3,480,000	11,800	77	5	16	—	—	2	
2-25-1929	70	3,648,000	8,600	80	6	14	—	—	—	
7-31-1929	55	2,850,000	7,400	77	1	18	—	2	2	" "
12-27-1928	Blood sugar 86 mg 2¼ hours after injection									
12-27-1928	Blood sugar 87 mg before injection    Blood urea nitrogen 9.3 mgs per 100 cc of blood									
12-31-1928	Blood urea nitrogen—10.6 milligrams									
1- 2-1929	Blood sugar—79 milligrams    Before injection									
1- 3-1929	Blood sugar—89 milligrams 24 hours after injection									
1- 5-1929	Blood sugar—86 milligrams									
1-17-1929	Blood urea nitrogen—12.1 milligrams									
2- 5-1929	Blood urea nitrogen—8.8 milligrams									
2-14-1929	Blood urea nitrogen—10.2 milligrams									

*Urmalayss* Traces of albumin on 12-28-1928, 12-29-1928, 12-31-1928, 1-3-1929, 2-5-1929, 2-6-1929, 2-8-1929, 7-30-1929

intercostal spaces could be felt numerous hard, immovable nodules A radiograph of the chest was reported by Dr Herendeen as showing extensive metastases in the right base, with thickened pleura, fluid and involvement of the lung parenchyma

*Course*—Within 30 minutes after each injection the patient had a chill lasting an hour or more, within three hours after injection her temperature rose to 103°F In three instances there was nausea and vomiting shortly after the injection The patient stated she felt better after each treatment, but no objective improvements were discerned In March, 1929, there were vertebral metastases In May, 1929, her liver was greatly enlarged and nodular and there was bilateral hydrothorax On July 30, 1929, — 650 cc of sanguineous fluid were withdrawn

from the right pleural cavity In July, she menstruated three times for seven days each She died on August 3, 1929 A necropsy was performed, the anatomical diagnoses were —

- (1) Recurrent carcinoma of the right breast with metastases to left breast, left axilla, pleura, lungs, bronchial lymph nodes, both adrenal glands and bone
- (2) Right hemothorax with atelectasis of the right lung
- (3) Congenital anomaly of duodenum and gall-bladder
- (4) Bilateral papillary tumors of ovaries
- (5) Subserous fibroid tumor of uterus

On microscopical study, the breast cancer was a cellular adenocarcinoma

Intravenous administration of colloidal silver solution

- 12- 1-1928—17 milligrams of colloidal silver in 93 cc of solution
- 12- 7-1928— 9 milligrams of colloidal silver in 41 cc of solution
- 2-25-1929—30 milligrams of colloidal silver in 110 cc of solution

Laboratory Examinations —

12- 6-1928—Gastric analysis—No free hydrochloric acid 2½cc total acidity  
—Gastric contents contained many groups of large hyperchromatic cells, probably cancer cells

Blood Counts	Hb	R B C	W B C	Poly Neut	Large Lym	Small Lym	Trans Cells	Eos	Bas
11-21-1928	75	3,640,000	13,200	56	7	27	5	3	2
11-30-1928	80	4,000,000	9,400	74	7	13	1	4	1
12- 1-1928	75	3,800,000	13,600	83	4	11	1	1	occasional stippled cell
12- 6-1928	78	3,920,000	12,200	77	13	4	6		
12- 8-1928	75	3,800,000	11,600	74	2	20	3	1	1 stippled cell
12-27-1928	70	3,600,000	11,000	68	7	20	2	3	
2-25-1929	80	4,200,000	14,600	85	4	11	—	—	—
12- 1-1928	Blood urea nitrogen—11.3 milligrams per 100 cc of blood								
12- 8-1928	Blood sugar—128 milligrams per 100 cc of blood								
12-10-1928	Blood urea nitrogen—10.2 milligrams per 100 cc of blood								
2-25-1929	Blood sugar—167 milligrams per 100 cc of blood (before injection)								
2-25-1929	Blood sugar—173 milligrams per 100 cc. of blood (24 hours after injection)								

12- 3-1928—Numerous analyses over four months time were normal except for two in-  
12- 3-1928 traces of albumin on Dec 4 and Dec 10, 1928

The ovarian tumors were simple benign papillary adenomas

*Case Report No 2* I L, a Russian Jewish tailor, aged 50 years, was admitted to the Memorial Hospital on Nov 21, 1928, with the complaint of severe indigestion of six months duration. His symptoms were,—anorexia, gaseous eructations, nausea and vomiting of increasing frequency, constipation, progressive asthenia, profuse nocturnal perspiration, indefinite visual disturbances, heaviness in epigastrium, loss of seven pounds in weight, hematemesis once and melena once

The patient was an anemic middle-aged Jew. The lungs and heart were normal to physical examination. The only positive finding was a resistance and a sense of fullness in the epigastrium. The liver was not palpable. After a barium feeding, a radiograph of the stomach revealed an extensive carcinoma of the gastric fundus involving both curvatures, no retention was found in the six hour film.

*Course*—After the first injection of colloidal silver, he had a slight chill followed by a fever of 101°F, and vomiting. His appetite improved and

after the second treatment his weight had increased by 17 pounds, his red blood count was higher than at any previous time. This improvement was transient. Later radiographs demonstrated that the carcinoma had increased in size to involve three-fourths of the fundus. The patient died on June 25, 1929.

*Case Report No 3* C S, a white widow, aged 52 years, was admitted on Dec 21, 1928, complaining of backache, urinary distress and sanguineous vaginal discharge. She had one adult child. Her menopause was at age 40. Two years prior to her visit, she first observed an occasional "spotting" of blood. In Sept, 1928, she had a severe uterine hemorrhage lasting one week, followed by a constant bloody purulent discharge. She had some difficulty in starting the urinary stream during the two weeks prior to her application. For one year, she experienced a severe sacral backache. She had lost no weight.

The patient was an anemic middle-aged Irish woman. The heart and lungs were normal to physical examination. The liver margin extended one finger breadth below

#### Intravenous administration of colloidal silver solution

12-19-1928—22 milligrams of colloidal silver in 85 cc of solution

12-24-1928—20 milligrams of colloidal silver in 82 cc of solution

#### Laboratory Examinations —

Blood Counts	Hb	R B C	W B C	Neut	Large Lym	Small Lym	Trans Cells	Eos	Bas	Fragile
12-18-1928	75	3,600,000	11,900	79	3	11	—	4	1	3
12-24-1928	60	2,920,000	9,400	88	4	3	3	—	2	—
12-26-1928	75	3,940,000	11,000	83	2	12	2	1	—	—
12-19-1928	Blood sugar—99 milligrams per 100 cc of blood (before injection of silver)									
	Blood urea nitrogen—8.5 milligrams per 100 cc of blood (before injection of silver)									
12-19-1928	Blood sugar 90 milligrams six hours after injection									
12-20-1928	Blood sugar 93 milligrams per 100 cc of blood 30 hours after injection									
12-26-1928	Blood urea nitrogen—12.2 milligrams per 100 cc of blood									
12-24-1928	Blood sugar 95 milligrams per 100 cc of blood before injection									
	Blood sugar 95 milligrams per 100 cc of blood 2 hours after injection									
12-27-1928	Blood urea nitrogen 12.1 milligrams per 100 cc of blood									
12-29-1928	Blood sugar 90 milligrams per 100 cc of blood									

*Urinalyses*—Albuminuria was practically constant, but slight in amount

the costal margin The cervix uteri was barely palpable, it was entirely replaced by diffusely growing carcinoma The entire pelvis seemed to be infiltrated with cancer tissue producing the condition known as "frozen pelvis" By rectal digital examination, densely immovable parametrial infiltrations were palpated

*Course*—After each injection of colloidal silver, she had a slight chill followed by a fever of 102°F No improvement was observed. The uterine bleeding increased in amount, she became progressively more anemic and weaker She died on January 18, 1929

*Case Report No 4.* L. D., a married woman, aged 46, had her left breast removed for cancer at the Brooklyn Hospital in January, 1929 On admission to the Memorial Hospital, April 15, 1929, recurrent tumor masses were found in the operative scar and in the left axilla There were also hard palpable lymph nodes in the left supraclavicular space and left cervical region There was definite tenderness over the lower three ribs in the right mid-axillary line. Radiographs on April 15, 1929, and June 24, 1929, were reported by Dr Herendeen as showing evidence of metastasis to spine, chest and pelvis with extensive bone

involvement The diagnosis was recurrent inoperable carcinoma of left breast with widespread metastases

In April, 1929, the left chest anteriorly and posteriorly were treated by low voltage x-rays and the supraclavicular spaces and axillae were treated by high voltage X-rays. In July, two high voltage X-ray treatments were given to the pelvis posteriorly

*Course.*—There was no beneficial influence in the course of the disease The skin metastases became numerous The liver became greatly enlarged and nodular, extending to the costal margin In December, 1929, a pathological fracture of the neck of the left femur occurred The patient became emaciated The red blood count increased slightly

*Case Report No 5* A. B., an Irish widow, aged 58 years, was admitted to the Memorial Hospital on Oct 26, 1926, for prophylactic X-ray treatment following left radical mastectomy She had eight children, none of whom had nursed the left breast because of a retracted nipple In May, 1929, she first felt a lump in her left breast, in Sept, 1929, the radical mastectomy was done at another institution

The only evidence of mammary cancer found on admission was a palpable lymph

#### Intravenous injection of colloidal silver solution

8- 7-1929—203 milligrams of silver in 90 cc of solution

9- 5-1929—29 milligrams of silver in 110 cc of solution

12-14-1929—238 milligrams of silver in 100 cc of solution

#### Laboratory Examinations —

10-15-1929—Pathological Report Small-cell infiltrating cellular tubulo-alveolar carcinoma Grade III—radiosensitive

Blood Counts	Hb	R B C	W B C	Neut	Bas	Eos	Trans Cells	Large Lym	Small Lym
8- 7-1929	75	3,900,000	5,400	84	—	2	1	3	10
8-12-1929	75	3,970,000	3,800	84	—	1	—	2	13
9- 5-1929	80	4,200,000	4,200	87	—	—	—	6	7
12-14-1929	85	4,320,000	7,800	84	—	—	1	6	9
12-17-1929	85	4,400,000	7,200	84	—	—	—	2	14
12-17-1929	Blood urea nitrogen—10 milligrams per 100 cc of blood								

*Ur. studies.* Albumin present in moderate quantities on 8-7-1929, 8-8-1929; 9-5-1929, 9-7-1929, 12-14-1929, 12-17-1929, 12-17-1929 Hyaline casts present on 12-14-1929.

node in the left supraclavicular space. One post-operative low voltage x-ray cycle was given to the left chest, left axilla and left supraclavicular space. The left supraclavicular space received 3 additional x-ray treatments in 1927 and two in 1928. On April 19, 1928, a radiograph of the chest was reported as showing mottling in the parenchyma of the lungs on both sides and enlarged hilus glands. By July 29, 1929 the lungs were studded with metastases.

3 The introduction of the colloidal silver induced no discernible changes in the composition of the blood and urine. These findings contradicted the reports of other investigators that colloidal silver induced a hypoglycemia when administered intravenously.

4 Microscopical study of one of these carcinomas removed at necropsy

Intravenous administration of colloidal silver solution

8-29-1929 30 milligrams of colloidal silver in 117 cc of solution

*Laboratory Examinations*—Urinalysis repeatedly normal

8-29-1929—Blood count—3,950,000 Red Blood Cells per cu mm of blood Hemoglobin—75% 7,000 White Blood cells per cu mm of blood Differential count—66% neutrophils, 3% large lymphocytes, 27% small lymphocytes, 2% transitionals, 2% eosinophiles

8-30-1929 Blood sugar—101.4 milligrams Blood urea nitrogen—86 mgs per 100 cc of blood

*Course*—From Aug 1, 1929, to Oct 21, 1929, the patient lost 40 pounds in weight. There was no appreciable effect produced by the constitutional treatment. The patient is at present bedfast.

## COMMENT

1 Five cases of inoperable cancer were selected for treatment by colloidal silver. Of these, 3 were mammary carcinomas, one was gastric carcinoma, and one was carcinoma of the cervix uteri.

2 The intravenous injection of colloidal silver solution provoked an immediate but temporary systemic reaction, consisting of chill, fever, nausea and vomiting. This constitutional reaction limited the amount of metallic colloid injected at a single dose to 30 milligrams.

(Case No. One) showed no histological evidence of any influence of colloidal silver on the carcinoma cells or tumor stroma.

5 There were two instances of temporary subjective improvement which were probably due to the psychic influence of the intravenous medication, one patient gained in weight. There was never any actual decrease in size of any of the tumor masses. The progress of the disease appeared to be unaltered.

6 It is probable that the occasional beneficial result obtained in cancer therapy by the use of colloids of heavy metals, notably lead, is not due to their biologic action as foreign colloids per se, because a similar colloid, namely silver, produces no demonstrable effect on the growth of cancer in the human.

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# A Cheaper Source of Oxygen

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**T**HE increasing use of oxygen inhalation for long periods in hypoxemic states, and the considerable expense attendant upon the prolonged administration of oxygen from tanks under pressure, emboldens me to report a very inexpensive source of oxygen which is available in practically all large cities

The now widely used Linde process for the manufacture of oxygen consists of the compression and fractional release of compressed air on a progressive plan leading to the liquefaction of air at a temperature of — 190 C. This liquid when exposed at atmospheric pressure rapidly gives off its nitrogen, since the boiling point of this gas is considerably higher than that of oxygen, and pure liquid oxygen, a thin, watery, pale blue liquid remains. At room temperature it is of course always in violent ebullition, and gaseous oxygen escapes constantly from any vessel in which the liquid is contained. This gaseous oxygen is of the highest purity, and complies with all specifications for "Medical Oxygen." Any attempt to confine it is futile and dangerous, and attendants must be warned not to attempt to shut off the flow of gas.

An ordinary steel vacuum bottle of two quart capacity filled with liquid

oxygen gives off gaseous oxygen at the rate of about one liter per minute, which rate may be accelerated by shaking the bottle, or, in case a rapid continuous flow of gas is desired, by employing a non-insulated container. Glass bottles, unless of very thin walls, are prone to break when subjected to this very low temperature. A perforated rubber stopper and tube leads the gas to a small wash bottle which serves only to visualize the flow of gas, and the effluent from the wash bottle goes to the patient who receives the gas from a mouthpiece, or by inhaling it from under a small tent into which the gas is allowed to escape. The tendency to apnoea from hyperoxemia when observed may be controlled by the occasional admixture of carbon dioxide from a pressure tank being allowed to enter the tent. The relative proportions of the gases may be controlled with sufficient accuracy by comparing the streams of bubbles through the wash bottles. We employ a tent of pyramidal shape with a square base 3 feet on a side and 2 feet high. A heavy wire frame supports a cover of heavy unbleached muslin. In each of the 4 sides is a window 14x17 made of a cleaned x-ray film. A flounce 8 inches wide surrounds the base, and is tucked under pillows and bedding.

One volume of liquid oxygen gives off approximately 800 volumes of gaseous oxygen, and the local price, which is probably higher than in mainland cities, is one dollar per quart, or one dollar for 200 gallons of gaseous oxygen. By comparison of this figure with the price of compressed oxygen in your community the effected saving may be estimated

Gas products supply-houses furnish gallon size or larger insulated containers which may be used as reservoirs for the liquid, from which the vacuum bottle may be filled as needed. The larger the bulk of liquid the slower the relative rate of evaporation, and a gallon will not be exhausted for several

days. Pouring the liquid from one container to another results in the formation of dense clouds of visible water vapor, and the process looks dangerous, but is not. Contact of the skin with the liquid for more than an instant will, of course, result in frost bite, however.

Undoubtedly this source of oxygen is already being widely employed, but I have not encountered mention of it in the literature. It has been used by us for more than two years with perfect satisfaction. Naturally it is not adapted to emergency use, since, as the Scotchman said of whiskey, "It won't keep."

## Editorials

### ON CANCER CURES

The one encouraging sign of the present widespread discussion of an alleged cancer cure is that there seems to be developing a certain ethical sense as to the propriety of making any statement as to the supposed curative powers of any method of treatment of cancer whatsoever. During the last forty years we have seen an almost annual exploitation of "cancer cures" which have had their brief season of notoriety and public attention, and then failing, as all have failed and must fail, are passed along into the discard of oblivion. The path of progress of medical knowledge is strewn with abandoned cancer-cure wreckage of every kind and description. In a general way such cancer cures reflect the ideas of cancer etiology prevailing at the time. In the nineties of the last century and in the first decade of the present one the predominant idea as to the cause of cancer was that cancer was an infectious disease and that ultimately some specific cancer organism must be found. When found, cancer therapy would naturally resolve itself into the attempt to conquer the organism or to abrogate its action upon the body by means of antibacterial or antitoxic methods and means. It was natural that at the outset a certain analogy between cancer and infectious disease should have been thought to exist. The origin and

manner of growth of neoplasms suggested in many ways the action of a parasite, and the bacteriological stage of cancer investigation was a logical and necessary one in the attainment of the knowledge of the nature of cancer which we now possess. Every form of micro-organism known to science practically has at one time or other been regarded as a possible cancer cause. There have been cancer cocci, bacilli and spirilla figured and described, cancer yeasts and moulds have had their little day of etiologic prominence, and finally various organisms regarded as protozoa have had beautiful cycles of development illustrated in minute detail. In this connection the mistaken diagnosis of cork cells as cancer parasites may be recalled. And we just missed the possibility of including round worms and a species of taenia as specific agents of tumor etiology in the form of *Spiroptera neoplastica* and *Taenia crassicolis*. Fortunately, the experimental rôle played by these verminous parasites in the production of animal neoplasms came along after the controlling part played by heredity and cancer susceptibility in the development of neoplasm had become known to us, so that no specific agency was attributed to these worms as etiologic agents of cancer. By the end of the first decade of this century experimental animal work, together with the fuller bacteriologic and

pathologic studies of neoplasm had convinced us that cancer is not an infectious disease, and that no specific living agent exists for the production of cancer, and that the part played by living organisms in the development of neoplasm is but purely that of a secondary, non-specific extrinsic factor of irritation, which will have no effect in the production of neoplasm in any one not possessing an intrinsic cancer susceptibility or tendency. This knowledge is now generally accepted, and very few pathologists today regard the infectious theory of cancer as being any longer worthy of consideration. But still there will crop up among practitioners at large cancer-cures based on an unfounded premise of cancer as an infectious process. Mistaken conceptions regarding certain infectious growths in the lower animals, particularly the so-called Rous chicken sarcoma, have been in part responsible for the persistence of such views. By many workers the chicken sarcoma is regarded as an infectious granuloma, and not comparable to the true neoplasms of man. The last ditch of the infective theory for the etiology of neoplasm was that of Gye and Barnard, who invented an ingenious compromise between the infective and chemical theories of cancer etiology through the assumption of a *non-specific living* agent and a *specific chemical* substance, both of which are essential to neoplasm production. An assumption so far-fetched that it is amazing that it should have received any scientific consideration at all, and all attempts at the control of the Gye-Barnard work have been, as expected, wholly negative. There exists, there-

fore, today absolutely no proof that infection plays any specific exciting cause in the production of neoplasm, hence all cancer cures based upon such an assumption of etiology may at once be dismissed as outside the realms of possibility. No specific antibodies are formed in the bodies of cancer-patients, and all cancer-therapy in the form of serums and vaccines becomes at once theoretically impossible and practically worthless. No hope is to be held out for any curative or preventive method to be developed along these lines. This should dispose of all the cancer-cures based upon such ignorance of the actual pathologic situation; and the public should be educated as to this point, as well as the members of the profession. When once the public mind has become cognizant of the fact that cancer has no infective etiology, then much will have been accomplished to prevent cancer patients from falling victims to cancer cures. A second class of cancer therapy is based upon the equally false hopes of destroying the cancer cells within the body. In their earliest form such cures consisted in the application of caustic applications directly to the affected part. Zinc and arsenical pastes and other forms of corrosives were used for this purpose, and many patients suffered untold agony from the ulcerating and gangrenous sloughs produced by these applications, with the result of exacerbation of the growth, rather than an inhibition. The majority of the old-fashioned quack, Indian and herb cures for cancer were of this variety. Even today one meets with patients who are suffering from the use of cures reputed to "eat out

the cancer" While it is possible that certain superficial and sharply localized cancers might be destroyed by such destructive applications, such is usually not the case, and in no way can such methods be compared with those of clean surgical removal. Under the irritation of such methods cancers usually show an increased rate of growth. Moreover, the attempt to destroy neoplasms by the injection, either into their substance or into the body itself, of various lytic materials, meets with similar disappointment. A long list of such cancer-lytic substances has been tried out to no avail. It is a well known fact that the older portions of malignant neoplasms undergo degeneration and necrosis, and that almost anything injected into the neoplasm will aid in producing such regressive changes. Moreover, the spontaneous regression of neoplastic nodules may at times be so great that the nodules may be so reduced in size as to apparently disappear. Only in the case of malignant syncytioma has the spontaneous disappearance of a metastatic nodule been known to occur, but this neoplasm arising from chorionic epithelium must be considered in a class apart from those arising from the tissues and organs of the individual body. Moreover, the general effects produced by the injection of cancer-lytic material often add greatly to the tumor cachexia present, and the great majority of them only hasten the end instead of delaying it. Herein belong such substances as Coley's mixed toxins, extracts of various organs and tissues, sera and effusions from cancer patients, and various endocrinal preparations, such as the Coffey-Humber ex-

tract of adrenal cortex. It has long been known that necrosis of tissue would follow the injection of adrenal gland extracts, as for instance, gangrene of the abdominal wall in experimental animals. Such an action has in no case been shown to be specific for cancer cells alone, and the sad fact attending the use of all such lytic substances is that only the older portions of the neoplasm are affected and die, while the growth of the younger cancer cells is apparently only stimulated. At any rate rapid increase in the growth and spread of neoplasms is often seen as a result of their use. Precisely similar is the situation attending the use of the intravenous injection of colloidal preparations of the heavy metals, lead, gold, silver, copper, etc. Was no lesson learned from the Blair Bell colloidal lead fiasco? Any pathologist with only a rudimentary knowledge of general pathology should have been sure as to the ultimate failure of such a treatment, and of the falseness of the premises upon which the philosophy of this treatment was built. Why was Bell's statement as to lead being lytic for chorionic epithelium not challenged? There was absolutely no proof of such an action of lead upon the placental ectoderm, or of his interpretation of the action of lead in producing abortion. What was known of the vascular action of lead poisoning should have been sufficient to offset these unwarranted claims as to the specific destructive action of lead upon embryonal cells. And yet so curiously unbalanced is human psychology that a noted pathologist supported Bell's claims, just as a reputable journal of medicine uttered

glowing prophecies as to the important therapeutic significance of the Gye-Barnard fiasco. In such cases the conservative doubting pathologist finds himself too often in Cassandra's position, and is put down for a pessimistic prophet. His only satisfaction is that if he lives long enough he is sure to have the last laugh. But joking aside, this is all too serious a matter for even satisfaction at having correctly prophesied. None of the carefully controlled experimental work in this line has shown the slightest specific action of any of the colloidal metallic preparations upon the cells of neoplasm. To kill all of the cancer cells by any method of chemical therapy would mean the death also of the body cells, and what is most probable is, that they would die before the cancer cells, because of the greater emancipation of the latter from the general body metabolism and chemistry. It seems certain that nothing can be hoped for in the nature of any substance that injected into the body will kill all the cells of the parasite neoplasm and leave undamaged the cells of its host. The world is not built upon that line. It is not pessimism which makes us declare that a cancer cure of this nature will never be found, in the very nature of things it does not and cannot exist. And further, we may safely declare that a cancer-cure as such is beyond all probability of achievement. Cancer is not simply a local disease, as is a streptococcus boil; we know now that it is primarily a disease of the entire organism, an anomaly of the individual constitution. Moreover, a local organ or tissue predisposition is also neces-

sary for its development. The general constitutional anomaly determines whether an individual can have a cancer, the local organ predisposition determines the site of the cancer. Further, there is the external factor of irritation to be considered. We do not yet know whether this extrinsic factor can take the place of the local organ predisposition, but there appears to be some evidence to the effect that it can. The general constitutional cancer-susceptibility is an inherited one, although this inheritance may manifest itself in different forms in different families. Further, the members of a family possessing the cancer susceptibility do not all possess the same degree of strength of the cancer predisposition; in some the cancer may appear early and without the operation of the extrinsic factor, in other members of the same family the cancer susceptibility may not show itself until very late in life, or be brought out only through the action of the extrinsic factor. The number of cancer deaths must be very much less than the number of individuals possessing the cancer susceptibility, as many of the latter will die of other diseases before the cancer susceptibility can assert itself. If we can promise no specific cure for cancer what can we do to restrict its ravages. We may attempt to breed out the intrinsic cancer susceptibility, but that will take many generations of eugenic breeding. Against the development of the local organ predisposition there is much greater ground for hope. Congenital anomalies in the Cohnheim sense of misplaced tissues may be corrected or removed, and the extrinsic factors producing chronic

irritation favoring cancer development may be largely controlled or abrogated. Much can be done in this direction for the prevention of cancer development. And in the case of its development early diagnosis and complete and extensive surgical removal will tend to bring about more complete cures than we are seeing today. There is much room for advance along the lines of both early diagnosis and thorough removal. Conservatism as to the extent of operation in the removal of a primary cancer is the chief mistake made by surgeons in the treatment of cancer. With a better knowledge of the pathology of the different forms of neoplasm surgeons will cease to "shell out" neoplasms or to cut too closely to the border of an infiltrating growth. From the standpoint of the pathologist these are common errors of surgical technique. As to the curative results from x-ray and radium irradiation these methods of treatment of malignant

neoplasms have proved very disappointing. Particularly is the irradiation of the affected area after operative removal of the neoplasm now being advised against, as some workers believe that such irradiation favors the occurrence of metastases. To sum up, there is little or no chance of any specific therapeutic agent for cancer ever being found; therefore, the advertisement and exploitation of so-called cancer cures leads only to the tragic blasting of unwarranted hopes excited in the lay mind through such announcements. Would it not be much better to prevent such public calamities by the development of a strong ethical sense that would lead to the censuring of the premature announcement to laymen of all experimental work connected with cancer therapy? Such exploitation should be regarded as beyond the limits of medical ethics and of common decency.

## Abstracts

*The Etiological Rôle of Bacteria in Bile Peritonitis An Experimental Study in Dogs* By ALLAN G REWBRIDGE and L S HRDINA (Proc Soc f Exper Biol and Med, March, 1930, p 528)

According to the prevalent view "bile peritonitis" is due to the toxicity of bile. Horrall observed that when bile was allowed to drain continuously into the peritoneal cavity the dogs died within 24 hours. He attributed the cause of death to the toxicity of the bile salts. In order to gather additional data on the mechanism of "bile peritonitis" the following investigation was carried out. In a series of 20 dogs, peritonitis was produced by allowing bile to drain into the peritoneal cavity. Determinations of bilirubin by the Van den Bergh method and bile salts by the Pettenkofer reaction developed by Aldrich were made on blood drawn from the femoral veins of the dogs 4 and 18 hours after their operations. No increase of bilirubin or bile salts could be detected by these methods even though the animals were dying as the result of their peritonitis. At necropsy the peritoneum was inflamed, the surfaces covered with a thin layer of fibrin and a few small areas of fat necrosis were observed around the pancreas. The peritoneal cavity contained a serosanguinous exudate in which were observed polymorphonuclear leukocytes and Gram positive bacilli. This organism was cultured from the peritoneal exudates of all 20 dogs studied. Cultures of bile removed from the gall bladder at the time of operation were all sterile except one in which grew a short Gram negative bacillus. A 10 per cent solution of bile salts filtered through a Berkefeld filter, and shown to be sterile when introduced into the peritoneal cavity produced a peritonitis identical with "bile peritonitis," except that fat necrosis was more extensive. Of the 20 dogs in this experiment smears and cultures of the peritoneal exudate show-

ed the same Gram positive bacillus in 19. In one no growth occurred. Twenty c.c. of an 18 hour broth culture of this bacillus when introduced into the peritoneal cavity produced a peritonitis identical with "bile peritonitis" except that areas of fat necrosis were absent. From the peritoneal exudate the same Gram positive bacillus were absent. From the peritoneal exudate the same Gram positive bacillus was cultured. The bacillus, a strictly anaerobic organism grows readily in broth and produces stormy fermentation within 18 hours in milk. The colony is large on an anaerobic blood agar plate, varies its color from yellow to brown and is surrounded by a wide zone of beta hemolysis. It stains well with methylene blue and positively by Gram's method. It varies considerably in length, is broad, square ended and has an occasional subterminal spore. This organism is either *B. welchii* or some other bacillus closely related to it. These observations tend to show that "bile peritonitis" is an infection produced by *B. welchii* or some other anaerobic bacillus closely related to it. (The weak spot in this investigation is the autopsy demonstration of the supposed infecting organism. Postmortem invasion of the peritoneal cavity is not ruled out. Editor.)

*Effect of Diet on the Healing of Experimental Gastric Ulcer* By G B FAULEY and A C IVY (Proc Soc of Exper Biol and Med, March, 1930, p 531)

Ferguson was able to produce uniformly in rabbits gastric ulcers which persisted 2-8 months or longer. He incised the anterior wall of the stomach and at the point of incision removed a piece of the mucosa, and then closed the stomach by a silk suture, the rabbits being kept on a diet of hay, oats and carrots. It occurred to Fauley and Ivy that this observation provided a method of studying the effects of diet on the healing of this experimental ulcer. In the first series of



rabbits used they found that if a lesion was made in the posterior wall of the stomach in which no silk suture was present and the rabbits placed on the stock diet of hay, oats and carrots, that the posterior lesion healed in 30 days, but the anterior lesion did not. This showed that the silk suture was a factor in the delayed healing and that in the absence of the silk, diet played no rôle in delaying healing. Anterior lesions of the Ferguson type were made in 29 rabbits. Twelve were placed on the stock diet and 17 on a diet of milk, bread and mashed boiled carrots. The rabbits were sacrificed on the 30th day. All of the 12 rabbits on the rough diet had ulcers on the 30th day. Only 3 of the 17 on the "soft diet" had ulcers. The results show that the silk suture *per se* is not sufficient to prevent the ulcer from healing and that a "rough diet" plus the silk suture factor are sufficient to produce a chronic gastric ulcer, grossly and histologically, and that a "soft diet" favors the healing of gastric lesions. The same results were obtained in a series of 4 rabbits on a rough diet in which a gut suture was used in place of silk. In another series of 4 rabbits which were kept on a diet of dry "quick rolled oats" with a fiber content of only 14 per cent, the ulcers failed to heal. On opening the stomachs of these animals, the contents were found to be pasty and dry as that found on the rough diet. This indicates that the fluidity of the gastric contents is also a factor determining the healing of gastric lesions.

*Reflexes from the Gall bladder to the Heart*

By WILLIAM C. BUCHBINDER (Proc Soc of Exper Biol and Med, March, 1930, p 542)

The sudden release of bile obtained by incising the gall bladder of a decerebrated or ether-anesthetized frog is almost invariably attended by an abrupt change in the rate and character of beating of the heart. The first event is a transient arrest of the entire heart lasting between 1 and 10 seconds, almost always followed by a sinus bradycardia lasting from one-half to ten minutes. Subsequently there is a return to the initial rate of beating, although in a few instances progressive slowing, leading to ex-

cessive dilation and permanent arrest, have been observed. Not infrequently the first event to be noted is a transient acceleration which precedes the slowing. The heart appears to beat much more forcibly with the inception of the slower rate. The latent interval for the reflex is a fraction of a second to a second or more. Electrocardiograms made from base to apex show the cessation of activity of the sinus and ventricular portions of the heart followed by increased amplitude of R and a rather characteristic inversion of T. That the changes in the initial and final ventricular complexes are not directly associated with the reflex are to be found in the repetition of electrical effects, following an occasional sinus block which appears spontaneously after the resumption of a normal rate of beating. Such an effect is quite comparable to aberrant complexes following premature beats in mammalian electrocardiograms. Prolongation of the PR interval does not occur and an extrasystolic arrhythmia cannot definitely be determined in the electrograms. Atropinization, decapitation or section of the vagi prevent the reflex. In the frog, there is, therefore, a specific reflex from the gall bladder to the heart which appears to have a vagal origin. Katz has suggested that the characteristic inversion of T with the inception of a slower rate of beating may well be a vagal effect producing asynchronous cessation of electrical effects in a ventricle in which there is decreased conduction. Irritation of the gall bladder by thermal or other instrumental means does not produce the succession of events noted when the stimulus is adequate. Acute pressure changes in the extrahepatic ducts are thought to constitute an adequate stimulus for the production of the reflex. It has also been suggested that this may be the mechanism operating for the production of the arrhythmias frequently seen in the human with so-called gall bladder disease, especially cholelithiasis.

*The Serum Treatment of Pneumonia* By E. S. MILLS (Canad Med Assoc Jour, April, 1930, p 488)

Mills reports results on a series of 52 cases of pneumonia treated with Felton's serum, at the Montreal General Hospital.

While small, the results are in agreement with the favorable results already published in the larger clinics in New York. In the 52 cases treated with serum there were 6 deaths, a mortality percentage of treated cases of 11.5 per cent. During the same period there was 20 untreated cases with 10 deaths, a mortality percentage in the controls of 40 per cent. The mortality in 400 cases at Montreal General Hospital before serum treatment was begun was 25 per cent. As a result of this experience and of others it would seem that the serum has little effect on resolution, which pursues its regular course, neither hastened nor retarded. The one great and significant fact is that the mortality has been considerably reduced by the administration of Felton's serum.

*The Inhalation of Pure Oxygen in the Treatment of Disease* By JOHN H. EVANS  
(Canad Med Assoc Jour, April, 1930, p 518)

The therapeutic value of inhaling pure oxygen for long periods of time has not been investigated. Considerable research has been done on therapy with 40-60 per cent oxygen, but the range of 60-100 per cent has been avoided because of the fear of producing harmful results. Medicinal and commercial

oxygen is about 99.5 per cent pure. This is what is meant when the terms "pure" or "100 per cent oxygen" are used. Evans endeavours to establish that pure oxygen can be safely administered by means of the face mask or nasal inhaler in cyanotic patients continually, as long as the cyanosis persists, secondly that it is advisable to administer 100 per cent oxygen early in pneumonia, as soon as the diagnosis is made, and continuing it throughout the course of the disease, intermittently if there is no cyanosis, and continually if there is, thirdly that daily inhalations of oxygen are beneficial in a number of pathological conditions where there is no apparent lack of oxygen in the blood. As a result of his experience, he concludes, that the continuous administration of pure oxygen, by means of the face mask or nasal inhaler over a period of days, to anoxemic patients has been productive of only beneficial results. The early administration of pure oxygen in pneumonia is a potent factor in reducing the mortality rate. The administration of oxygen for one to several hours daily has proved beneficial in cases of cardiac decompensation, asthma, hay fever, influenza, extensive burns, pulmonary embolism and hyperthyroidism.

## Reviews

*Progressive Relaxation* A Physiological and Clinical Investigation of Muscular States and Their Significance in Psychology and Medical Practice By EDMUND JACOBSON, A M, Ph D, M D 429 pages, 68 figures The University of Chicago Press, Illinois, 1929 Price in cloth, \$5.00

The great importance of rest in the treatment of disease is generally recognized, but in spite of its importance the field has remained practically unexplored from a scientific standpoint. Rest has been found useful in treatment in all branches of practice. It is commonly prescribed in various acute and chronic infectious diseases, in the more severe metabolic and nervous disorders, in gastrointestinal and general systemic affections, in asthenia, and in a large variety of surgical conditions. While devoting much effort to the development of other forms of therapeutic measures, medicine has used this, her oldest remedy, wholly naively and with little attempt at systematic study. It is the hope of the author of this volume to draw attention to the problems of fatigue and rest, and to present a method that will interest the general practitioner, the internist and the surgeon, no less than the neurologist. During neurosis there is failure to relax, recovery by whatever route attained generally is characterized by a return to a fairly normal relaxed state. The author has sought to test directly the effects of cultivating relaxation during neurosis. He describes a method of relaxation to quiet the nervous system, including the mind. Because of reflex connections, the nervous system cannot be quieted except in conjunction with the muscular system. The whole organism rests as neuromuscular activity diminished. The possible range of usefulness of the method of relaxation described in the book should not be narrowly restricted to neurology, since it may conceivably be applied wherever rest is useful in the practice of medicine. The present

studies of relaxation were begun twenty years ago, and are still in an early stage. Further investigations are under way, and many more must follow on the various systems before the range of the physiological effects of relaxation and of the clinical applications can be fully stated. The author suggests that the term neuromuscular hypertension should largely replace the term neurasthenia, except perhaps in a relatively few instances where exhaustion can be actually demonstrated. Phenomena of neuromuscular hypertension occur in the guise of symptoms, causes or effects almost throughout the whole range of the practice of medicine and surgery, and the opportunity for a wide and varied application of a method of relaxation is suggested. The author describes a method of progressive relaxation which can be applied to the treatment of acute and chronic neuromuscular hypertension, states of fatigue and exhaustion, debility, toxic goiter, insomnia, alimentary spasm, chronic pulmonary tuberculosis and vascular hypertension. The fact is emphasized that in the general practice of medicine and surgery neuromuscular methods may be used along with diet, drugs, operation, and other therapeutic measures. The practitioner will find this book interesting and suggestive.

*The Conquest of Cancer* By Radium and other Methods By DANIEL THOMAS QUIGLEY, M D, F A C S, Instructor in Surgery in the University of Nebraska College of Medicine 539 pages, 334 illustrations F. A. Davis Company, Philadelphia, 1929 Price in cloth, \$6.00

This book is an extraordinary collection of pathological ignorance and misconceptions. The general character of the pathology is shown in the statement that old age "is a disease, due to the inroads of the chronic infections which the individual has picked up during his life time." The pathology of

neoplasm is of the same grade of value. The case made out for the value of radium in the treatment of cancer is far from being convincing.

*Clinical Obstetrics* By Paul T. Harper, Ph B., M.D., Sc D., F.A.C.S., Clinical Professor of Obstetrics, Albany Medical College. 629 pages, 250 figures, with legends and charts. F. A. Davis Company, Philadelphia, 1930. Price in cloth, \$8.00.

This book is concerned with the description of the natural phenomena of parturition, with detailed consideration of the abnormalities of pregnancy, labor and the puerperium to which frequency of occurrence and the responsibilities involved give prominence, and with exposition of the operative procedures applicable to them. It is assumed that the reader is well-grounded in fundamentals from textbook study, and that such knowledge has been broadened by familiarity with the works of reference and with current literature. In his introduction the author insists upon the importance of visualizing each and every process concerned. The book is a study of individual reaction to obstetrical problems as they have presented themselves to the author. In its telling an effort has been made to place principles involved over and above the procedures that might be carried out. Deductions that individual situations seem to warrant replace extended comment and multiplicity of views, and thus of necessity makes the account personal. The text is illustrated with simple diagrams having appropriate legends. They are intended to help the reader to visualize what is set down in order to make him see what it is the purpose of the writer to convey. Having acquired the habit of visualization the reader makes his own mental pictures. The book is written with the firm conviction that clinical proficiency depends upon an analytical attitude toward all that is seen, and upon ability to isolate fundamentals and to make logical deductions therefrom, rather than upon mere docility in following out the details of operative procedures. The obstetrical material of the book is complete, clear, and clearly presented in an attractive manner, which makes it interesting and valuable.

*The Sthenics* The Chord Invisible By SIR JAMES K. FOWLER, K.C.V.O., C.M.G., M.A., M.D. MacMillan and Co. Limited, London, 1930. 81 pages. Price in cloth, \$1.40.

This little volume deals with those human beings, men and women, who possess a more highly sensitized central nervous system than is common to the race. The author does not have in mind those whose characteristics are to be described as merely "neurotic" or "neurasthenic," "highly strung" or as possessing the "artistic temperament," all of whom can easily be distinguished by a characteristic facies, or appearance or a manner which enables the trained observer within a few minutes to place them in their class. On the other hand a study much closer and more prolonged than this and a knowledge far deeper is required to recognize and unravel the very diverse and usually complex character of the type which the author has in mind, and which he styles the Sthenics or Hypersensitives. The positive characteristics of these it is not easy to define. Each one will be the result of a different heredity, and necessarily each will differ from all the others in some respect. They present great variety in physique, mentality, ability and temperament. In spite of these differences they present in common some qualities or mental characteristics by which they may be identified. The most obvious of these is the manifestation of vitality to an unusual degree, an interest in many things, and a capacity for sharing in the interests of others, a fertile imagination, which leads to the evolution of many schemes, of which, perhaps, a few only come to maturity. Their clearness of vision leads them to see the thing as it will appear when complete, before it is begun, and to overlook the difficulties which lie in waiting between inception and completion, and the necessity of securing the co-operation of many interests. In early life it may be obvious that they possess ability which may lead to distinction, and somewhat later these hopes are partially realized, usually, however, performance falls somewhat short of promise, some obstacle within preventing the attainment of the degree of success which was expected. High

attainment, tempered by relative failure, may persist throughout life, and the former may so overshadow the latter that it is not apparent. The element of failure is either not recognized, or, if so, is soon forgotten. Sound judgment, the greatest of faculties, is lacking, and this is apt to mar the whole. They are inclined to be ruthless in order to attain the end in view. They are essentially solitary workers and most suited for one-man jobs. They are not good judges of character. They tend to be inconsiderate in conduct toward subordinates. Socially they are always interesting, often brilliant and attractive, their presence acts as a stimulant to others on whom they are able to impart some of their stock of vitality. Their memory may be prodigious, and the variety of subjects upon which they are able to speak with a full knowledge is one of the factors which go to the making of a personality to which all are drawn. Among their physical characteristics is hypersensitiveness of the skin and mucous membranes. When ill they do not make good patients. They react badly to operations, with extreme restlessness and irritability. They are subject to spasms originating in some source of irritation and involving a limb and part of the trunk. Sthenics have been concerned in all the great friendships and the great quarrels of history. The author believes that Napoleon was a sthenic and not an epileptic. He also places Lord Curzon and Sir Edward Marshall Hall in this group. In conclusion he explains the sthenic individual on a biochemical basis of an over-secretion of adrenin.

*The Principles of Bacteriology and Immunity*. By W. W. C. TOPLEY, M.A., M.D., M.Sc., F.R.C.P., Professor of Bacteriology and Immunology, University of London, and G. S. WILSON, M.D., M.R.C.P., D.P.H., Reader in Bacteriology and Immunology in the University of London, London School of Hygiene and Tropical Medi-

cine. Two Volumes, 1300 pages, 241 figures. William Wood and Company, New York, 1929. Price in cloth, \$15.00.

Volume I treats of General and Systematic Bacteriology, Volume II of Infection and Resistance and the Application of Bacteriology to Medicine and Hygiene. The authors have attempted, on the basis of their personal experience in postgraduate and undergraduate teaching, to provide a textbook which will be of service to those students of medicine and biology who wish to make a serious study of bacteriology and its application to the problems of infection and resistance. The order of presentation is logical, the student should gain some knowledge of bacteria as a distinctive class of living things, and of their systematic relationships and ecology, before considering their reactions with more highly differentiated organisms. To bring the material within a reasonable compass, all detailed descriptions of technique have been omitted. The available evidence in each case is presented, no attempt has been made to simplify the issues by limiting the material of the book to well-attested facts or to undisputed conclusions. Both sides of the disputed and unsettled problems of bacteriology are presented. Literature is given at the close of each section. The material presented appears to be fairly well brought up to date, and is clearly and concisely stated. The illustrations are only fair. The chapter on bacterial variation is inadequate, because of the great prominence of this subject at the present time. As this is a very living matter of bacteriologic discussion, it should have been more completely treated. The authors apparently accept the legend of the importation into Europe of syphilis by the Columbian crews. The work of the Dicks on scarlet fever is quite thoroughly reviewed. Tularemia is included in the list of diseases of man, but undulant fever does not appear in the index. On the whole, these two volumes offer a well-rounded survey of modern bacteriology, brought up to date.

## College News Notes

### COLLEGE NEWS NOTES

Dr Howard L Hull (Fellow), Elma, Washington, addressed the Tuberculosis League of Benton County, on March 26, on the subject "Tuberculosis in Childhood" He addressed the Kittitas County League on the same subject on March 27, and the Yakima County League on March 28

Dr W W Britton, who has been for twelve years with the Homan Sanatorium, has become Medical Director of the Southern Baptist Sanatorium, El Paso, Texas Dr Britton succeeds Dr J D Riley, who has been elected Superintendent of the Arkansas State Sanatorium at Booneville The Southern Baptist Sanatorium is a regular advertiser and exhibitor with the American College of Physicians

At the meeting of the Dallas Southern Clinical Society on April 14, the following Fellows of the College delivered addresses

Dr Francis M Pottenger, Monrovia, Calif

Dr Logan Clendenning, Kansas City, Mo

Dr A B Moore, Rochester, Minn

Dr C C Sturgis, Ann Arbor, Mich

Dr Ralph Pemberton (Fellow), Philadelphia Orthopaedic Hospital and Infirmary for Nervous Diseases On March 14, he addressed the medical section of the Rutgers University Club at New Brunswick, New Jersey, and on March 26, he delivered one of the Wednesday addresses of the Fifth Avenue Hospital, New York City

Dr Arthur C Brush (Fellow), Brooklyn, is Consulting Neurologist to the Coney Island Hospital

Dr Emil Koch (Fellow), Brooklyn, is President of the Staff Society of the Bush-

wick Hospital Other Fellows of the College who are members of the Bushwick staff are Dr Joseph F Paulonis, Dr. Morris Weissberg and Dr Charles Eastmond, all of Brooklyn

Dr C S Danzer (Fellow), Brooklyn, has been appointed Attending Physician to the Cumberland Hospital, Brooklyn, Department of Public Welfare, City of New York

Under the Presidency of Dr Walter E Vest (Fellow), Huntington, the West Virginia State Medical Association will hold its annual meeting at White Sulphur Springs, May 20-22

Dr Sydney R Miller and Mr E R Loveland, President and Executive Secretary, respectively, of the College were guests at a luncheon given by Dr L B McBrayer (Fellow), Secretary and Treasurer of the Medical Society of the State of North Carolina, at Pinehurst on April 29 During the annual meeting of that society, Dr McBrayer initiated a sectional meeting of all of the Fellows and Associates of the College from the State of North Carolina This plan has proven very beneficial in getting members of the College acquainted with one another, and to foster pleasant associations among our members in stated localities

Dr Horton Casparis (Fellow), Professor of Pediatrics at Vanderbilt University, Nashville, addressed the semi-annual meeting of the Southwestern Virginia Medical Society at Radford (Va ), March 24-25

Dr LeGrand Kerr (Fellow), Brooklyn, is the author of a treatise on the subject "A Contribution to the Cause of Universal

Peace," which is said to have been responsible for the adoption of a joint resolution in the House of Representatives for the establishment of a Peace College. The resolution provides "that the President in his discretion appoint five persons, one of whom shall be a member of the Senate, one of whom shall be a member of the House of Representatives, one of whom shall be the President of a well-recognized University, one of whom shall be an industrialist, and one of whom shall be a member of the armed forces of the United States, to constitute a Committee for the purpose of conference and study to the end that its members may discover the best ways and means whereby the United States Government can establish an institution to be hereafter known as the United States Peace College, same to be situated in the City of Washington, District of Columbia." The resolution further provides an appropriation of \$100,000 to be used by this Committee in its study and research, and to report to both Houses of Congress its findings and conclusions.

Dr Joseph F Paulonis (Fellow), Brooklyn, is President of the Brooklyn Pediatric Society.

Dr Stuart Pritchard (Fellow), Battle Creek, addressed the Indianapolis Medical Society and the Marion County Tuberculosis Association, April 8, on the subject, "Significance of Cough."

Dr John Severy Hibben (Associate), Pasadena, addressed the Pacific Physiotherapy Association, March 26, on "The Visible Spectrum and Infra-Red Frequencies."

Dr Daniel N Silverman (Fellow), New Orleans, was elected President of the New Orleans Gastro-Enterological Society, January 23.

Dr Robert A Peers (Fellow), Colfax, Cal, and Dr Henry Chesley Bush (Fellow), Livermore, Calif, addressed the California Tuberculosis Association at Merced,

April 7-8, on "Blood Sedimentation in Tuberculosis" and "Parenchymatous Lesions in Childhood," respectively.

Dr Alphonse McMahon (Fellow), St Louis, addressed the Central Illinois Medical Association at Decatur, Illinois, March 25, on "The Heart in Hyperthyroidism."

Dr Leroy Sante ((Fellow) and Dr Jacob J Singer (Fellow), both of St Louis, addressed the St Louis Medical Society, March 25, on "Use of X-Rays in the Detection of Chronic Lung Suppuration" and "Tumors of the Chest," respectively.

Among the speakers at the one hundredth annual meeting of the Tennessee State Medical Association at Nashville, April 8-10, under the Presidency of Dr Leon T Stern (Fellow), Chattanooga, the following Fellows delivered addresses:

Dr Hugh C Cumming, Surgeon General, U S Public Health Service, Washington

Dr James S McLester, Birmingham

Dr Walter C Alvarez, Rochester, Minn

Dr Henry J John (Fellow), Cleveland, spoke before the Academy of Medicine of Cincinnati, March 10, on "Diabetes."

Dr John H Musser (Fellow), New Orleans, was the principal speaker at the banquet of the Birmingham Clinical Club, recently.

Dr Harold W Dana (Fellow), Boston, on March 7, 1930, was appointed Visiting Physician to the Boston City Hospital, being promoted from the position of Assistant Visiting Physician.

Dr Orlando H Petty (Fellow), Philadelphia, is the author of an article, "Treatment of Diabetes," which appeared in the March issue of the Pennsylvania Medical Journal.

The fifty-seventh annual meeting of the Northern Tri-State Medical Association was held at Fort Wayne, April 8. Among the speakers and their subjects were

Dr Robert M Moore (Fellow), Indianapolis

"Observations on Heart Diseases"

Dr Chester W Waggoner (Fellow), Toledo

"Economic Side of Medicine"

Dr Charles A Elliott (Fellow), Chicago

"Treatment of Liver Diseases"

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Dr David P Barr (Fellow), St Louis, addressed the St Louis Medical Society on March 18 on the subject, "Chronic Types of Arthritis"

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Dr Paul Dudley White (Fellow), Boston, addressed the Norfolk (Virginia) County Medical Society, February 17, on "Prevention of Heart Disease"

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Dr Clarence A Smith (Fellow), Seattle, addressed the King County Medical Society of Washington on April 7 on "Galvanic Therapy"

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Dr Charles A Elliott (Fellow), Chicago, delivered a paper before the North-eastern Indiana Academy of Medicine at Kendallville, February 27, on "Treatment of Hepatic Disease"

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At the twenty-sixth annual meeting of the Council on Pharmacy and Chemistry of the American Medical Association in Chicago, March 7-8, the following Fellows of the College, who are members of the Council, were present

Dr Torald Sollmann, Vice Chairman of the Council, Professor of Pharmacology and Materia Medica, Western Reserve University, School of Medicine

Dr W McKim Marriott, Professor of Pediatrics, Washington University, School of Medicine.

Dr W. W Palmer, Bard Professor of Medicine, Columbia University, College of Physicians and Surgeons

Dr Ernest E Irons, Clinical Professor of Medicine and Dean, Rush Medical College

Dr. A J Carlson, Professor of Physiology, University of Chicago

Other Fellows of the College who are members of the Council include

Dr George W McCoy, of Washington, D C, and Dr Leonard G Rowntree of the Mayo Clinic

Dr Julius Hess (Fellow), Professor and Head of the Pediatric Division, University of Illinois, College of Medicine, Chicago, has been appointed a member of the Council's newly established Committee on Foods

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Dr. William Gerry Morgan (Fellow), President-Elect of the American Medical Association, was one of the guests at the annual banquet of the George Washington University Medical Alumni Association on March 5

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Col Bailey K Ashford (Fellow), Professor of Tropical Medicine and Mycology, School of Tropical Medicine of Porto Rico, has been chosen by the Association of Military Surgeons of the United States as lecturer of the Kober Foundation for 1930. On March 28, Dr Ashford will deliver a lecture on "Significance of Mycology in Tropical Medicine" in Washington

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Dr Tracy R Love (Fellow), Denver, addressed the Northeast Colorado Medical Society, at Sterling, Colo, recently on "Gastric Disturbances and Diabetes Mellitus"

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Dr Shaul George (Fellow), Pittsburgh, spoke on "Treatment of Pneumonia" before the Allegheny County Medical Society on March 18

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Dr. George W McCoy (Fellow) of the U S Public Health Service, Washington, was one of the speakers at a symposium on psittacosis held by the Greater New York Public Health Officers' Association on March 25

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The Executive Secretary of the College announces the following gifts of publications by members to the College Library

One reprint, Dr B. S Pollak (Fellow), Secaucus, N J, "Ethical Hospital Concepts"



One reprint, Dr Samuel E Munson, (Fellow), Springfield, Ill, Hypertension "

Two books, "The Creed of A Biologist" and "Old Age," by Aldred Scott Warthun (Master), Ann Arbor, Michigan These books were contributed by Mr Paul Hoeber of New York City, the publisher

Seven reprints, Dr Thomas Klein (Associate), Philadelphia, Pa, "Agranulocytic Angina," "Abdominal Pain Resulting from Thoracic Lesions," "The Use of Coley's Mixed Toxins in the Treatment of Chronic Arthritis," "Syphilitic Splenomegaly Associated with an Osteomyelitis of the Clavicle," "Pulmonary Complications of Paratyphoid Fever," "Pulmonary Tuberculosis and Influenza," "Chronic Arthritis "

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The following additional gifts of reprints contributed to the College Library of publications by Fellows are acknowledged

Dr Frank Smithies (Master), Chicago, Ill

"Clinical Manifestations in Gall Bladder Disease A Study of 1000 Operatively Demonstrated Cases"

"Nonsurgical Drainage of the Biliary Tract" (With Karshner & Oleson)

"The Diagnostic and Therapeutic Value of Non-Surgical Biliary Tract Drainage in Patients Exhibiting Biliary Tract Disease Upon Whom Surgical Procedures Have Been Performed Previously" (With Oleson)

"Primary Carcinoma of the Gall Bladder"

"Gastro-Duodenal Hemorrhage"

"Advanced 'Hemolytic' or 'Pernicious' Anemia, Abscesses of the Roots of the Teeth, Chronically Infected Appendix and Gall Bladder, Splenitis and Perisplenitis"

"Deep Urethral Obstruction Caused by Carcinoma of the Prostate Resulting in Enormous Dilatation of the Urinary Bladder, General Arteriosclerosis, with Arterial Hypertension, Cardiac Hypertrophy and Interstitial Nephritis, Chronic Pancreatitis"

"Observations Upon the Nature, Diagnosis and Clinical Management of Gastric Ulcer"

"Epidemic Encephalitis (Sleeping Sickness', 'Lethargic Encephalitis,)', Chronic, Non-Active, Peptic Ulcer"

"Thrombosis of Cerebral Arterioles and Myocardial Inefficiency Producing Epileptiform Attacks, Infected Tonsils and Roots of the Teeth"

"Myocardial Weakness, Cardiac Dilatation, Paroxysmal Tachycardia,' Pulmonary Edema, Severe, 'Secondary' Anemia, Abscesses of the Roots of the Teeth and Obesity"

"Presidential Address" (American College of Physicians)

"A Treatment of Gastric Ulcer Based Upon Modern Clinical Histopathological and Physiological Investigations"

"On the Etiologic Relationship Existing Between Gastric Ulcer and Gastric Cancer"

"Symptoms and Signs of Gastric Cancer, an Analysis of 712 Consecutive Operatively and Pathologically Proved Cases"

"A Consideration of Factors Concerned in the Production and the Healing of Peptic Ulcer, with a Report of the Results of Treatment of 470 Patients by the 'Physiologic Rest' Regimen"

"The Clinical Significance of Vicarious Gastrorrhagia"

"Benign Pyloric Stenosis and Its Management"

"Non-Surgical Drainage of the Biliary Tract Its Usefulness as a Diagnostic and Therapeutic Procedure"

"On the Origin and Development of Ethics in Medicine and the Influence of Ethical Formulae Upon Medical Practice"

"Relationship of Infection to the Production of So-Called 'Pernicious Anemia' and its Significance with Regard to Treatment of Such Anemia"

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Dr Alvin E Siegel (Fellow), Philadelphia, Pa

"Typhoid Fever in Infancy"

"Respiratory Diseases of the New-Born"

"Pooled Adult Blood Serum as a Prophylactic Measure in a Measles Epidemic in an Institution."

## OBITUARY

PHILIP SEDDON ROY, M D

Philip Seddon Roy, one of the first to be accorded Fellowship in the American College of Physicians, (1916) died December 18, 1930. He was born in Tappahannock, Virginia, April 15, 1861. His father, Thomas Seddon Roy, and his mother, Fanny Burgess Micou, both died during his infancy.

After high school he graduated in 1880 from the Medical Department of the University of Virginia, at 19, and later took a post graduate course at Jefferson Medical College.

Dr Roy married Miss Alice Fitzhugh of Fredericksburg, October 23, 1890, who survives him.

Dr Roy practiced for a short time in Fredericksburg, Virginia, but in 1887 moved to Washington, D C, where he remained active until his last illness. Confining his work to internal medicine he was an authority on cardiovascular diseases. He published between twenty and thirty papers, the first "Heart Failure" appearing in the Journal of the American Medical Association, 1890. Preeminently a practical clinician, he was a deep student and constant reader. Sir James McKenzie was his ideal and he delighted in quoting him verbatim.

While always a regular attendant at Medical Society meetings, his interest in organized medicine really was crystallized after 1910, after which time he served as Vice President and later President of the Medical Society of the District of Columbia. He was also its delegate to the American Medical Association from 1914 to 1926 and

delegate, 1927 and 1928, Vice President of the Washington Academy of Sciences in 1918.

He was a member or fellow of the Medical Society of the District of Columbia, the American Medical Association, American College of Physicians, Medical Society of Virginia, Southern Medical Association, Medical History Club of Washington, American Therapeutic Society, Medical Society of Virginia, Maryland and the District of Columbia, Washington Academy of Sciences, University Club of Washington and the Colonnade Club of University of Virginia.

Those who met him at Association meetings, where he had friends by the hundreds, were perhaps most charmed with Dr Roy's geniality and wholesomeness. His little dinners of recent years to the President and President Elect of the American Medical Association will be long remembered.

Those of us at home think of his loyalty to friends, generosity, honesty and uprightness.

The loss of Philip S Roy to the profession was felt deeply by his fellow physicians and many patients when he died from angina pectoris in his sixty-ninth year.

(Prepared by J Russell Verbrycke, Jr, M D, F A C P)

Dr Edward Vernon Silver, a Fellow of the American College of Physicians, died at his home in New York on March 5, 1930.

Dr Silver was prepared for college at the Brooklyn Polytechnic Institute, at St. Johnsbury Academy, Vermont,

and finally at Phillips-Andover. He was active in the social life of his college, sang in the class glee club, and was a member of Delta Kappa.

He received his degree of Doctor of Medicine from Columbia in 1885. He then served as House Surgeon at the Roosevelt Hospital from 1886 to 1887, and studied in Vienna and elsewhere abroad the following year. From 1888 to 1891 he practiced in New York City, being connected with the Roosevelt Hospital and the Vanderbilt Clinic. From 1891 until his retirement about three years ago, he practiced in Salt Lake City, specializing in dermatology. He was Visiting and finally Consulting Physician to St Marks Hospital, and was a member of the Salt Lake City Board of Health. He was prominent in church affairs, being affiliated with the Presbyterian Church, and served in many social and public organizations identified with the interests of Salt Lake City. He was a fellow of the American Medical Association, the Salt Lake County Medical Association, and the Academy of Medicine.

Dr Silver was married in 1901 to Miss Bessie Larson of Salt Lake City. He was a twin brother of Dr Lewis M. Silver, and a cousin of Herbert B. Wilcox.

Dr Silver was a man of high repute both in and out of the profession, and throughout his entire life devoted himself most conscientiously to the welfare of his profession and his patients. He enjoyed a large and responsible practice, and was continuously identified with the best social and political life of his environment.

(Furnished by Dr Harlow Brooks, F A C P, Governor for eastern New York.)

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Dr James D. Love (Fellow), Jacksonville, Florida, died March 26, 1930, of pneumonia, aged 57.

Dr Love was born in Quincy, Florida, attended local and private schools in early life, graduated at the West Florida Seminary at Tallahassee with the degree of A. B., and in 1897 received his degree of Doctor of Medicine, as the honor man of his class, from the University of Maryland, Baltimore. He served one year internship in the obstetrical department of the University Hospital, and then located in Jacksonville, June 6, 1898, as a general practitioner. In 1909, he decided to devote his practice to pediatrics, and went to Vienna, Paris, London and Boston to prepare himself for this specialty. He did postgraduate study in Boston and New York during 1910 and 1911, and later in St. Louis. In 1913 and 1914, he began confining his activities to the diseases of children.

Dr Love was a member of the Duval County Medical Society, Florida Medical Association, Southern Medical Association, and had been a Fellow of the American College of Physicians since 1920. He had served as the Governor for Florida in the latter organization almost since the beginning of his membership. He was a member of the teaching staff of the Southern Pediatric Seminar, Saluda, N. C., a member of St. Luke's hospital staff since its organization, Consulting Pediatrician to the Duval County Hospital, Physician-in-Chief of Staff of

the Florida Children's Home, and a member of the staff of Riverside Hospital, Jacksonville. He had been President of the Duval Medical Society for two years, President of the Florida Medical Association, Secretary, Vice-Chairman and Chairman of the Pediatric Section in the Southern Medical Association. At the time of his death, he was alternate representative of the Florida Medical Association to the House of Delegates of the American Medical Association.

His contributions to medicine were many, he commanded the respect and the attentive hearing of every one at scientific meetings.

"His life was gentle and the elements  
were so blended in him

That all Nature might stand up, and  
say 'There was a Man!'"

(Furnished by Dr. R. H. McGinnis,  
F. A. C. P., Jacksonville.)

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Dr. John Garnett Nelson (Associate), Richmond, Virginia, died,

March 30, of abdominal carcinoma, aged 58 years. Dr. Nelson was elected to full Fellowship in the College on October 27, 1929, but due to his illness was never able to attend the Convocation and take up his Fellowship.

Dr. Nelson received his medical degree from the University College of Medicine in 1900, and at the time of his death was Professor of Clinical Medicine of the Medical College of Virginia. He was a prominent physician in Richmond for many years, and was well-known for his activities in connection with the Richmond Tuberculosis Association and as a leader of the McGuire Hospital unit during the World War. He was a member of the Richmond Academy of Medicine, a member of the Medical Society of Virginia, and a Fellow of the American Medical Association. The Medical College of Virginia, as a tribute of respect, suspended afternoon classes on the day of Dr. Nelson's funeral, in order that the faculty and students might attend.

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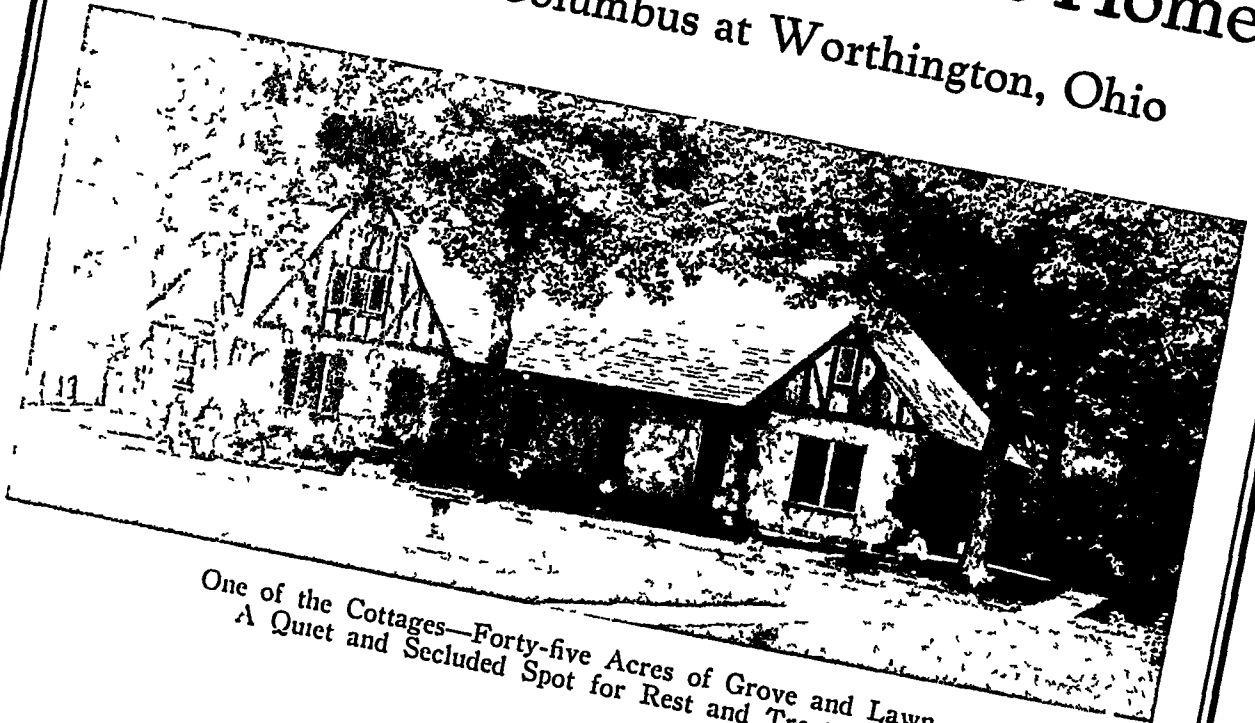
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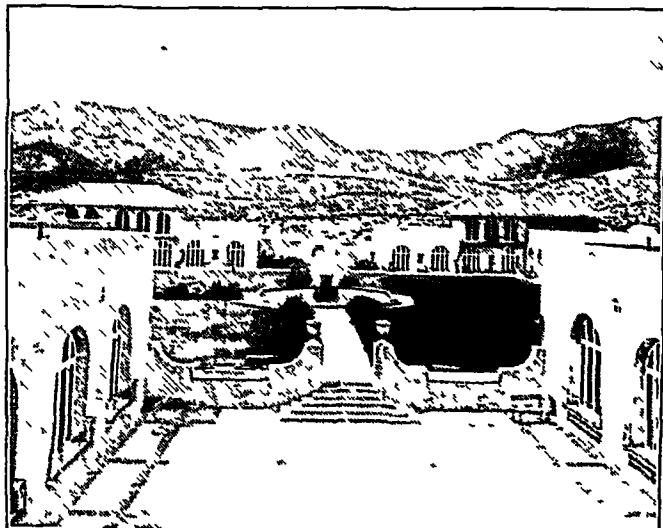
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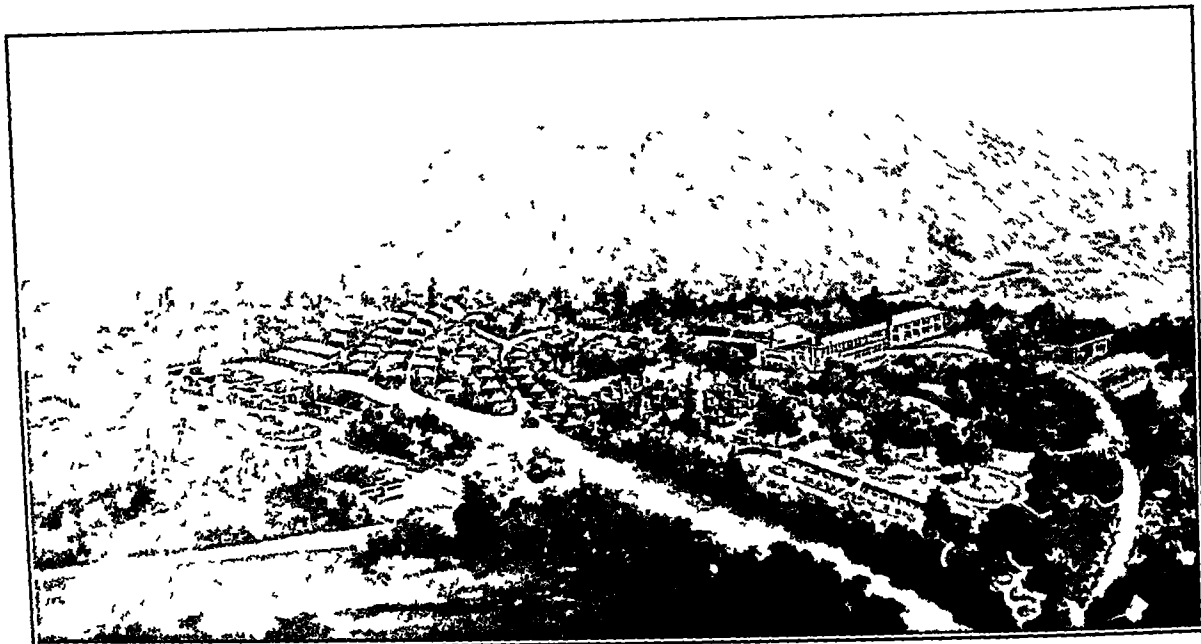
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